Access DB# 81573

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Deborah A. Davis Examiner # : 69897 Date: 12-3-02
Art Unit: 1641 Phone Number 308-4427 Serial Number: 09/913,707
Mail Box and Bldg/Room Location: 7D16 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Determination of Nuclease activity

Inventors (please provide full names): Stuart Harbron

Earliest Priority Filing Date: 2-20-99

***For Sequence Searches Only** Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

See attached Claims

Thank you.

****

STAFF USE ONLY

Searcher: Alexandra Waclawiw
Searcher Phone #: Technical Info. Specialist CM1 6A02 Tel: 308-4491
Searcher Location:
Date Searcher Picked Up: 12-9-02
Date Completed: 12-9-02
Searcher Prep & Review Time:
Clerical Prep Time:
Online Time:

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic ✓
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN $ 56.00
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

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10
1
55
86

PTO-1590 (8-01)

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     (FILE 'HCAPLUS' ENTERED AT 10:03:13 ON 09 DEC 2002)
               DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 10:06:51 ON 09 DEC 2002
               E NUCLEASE/CN
L1           1 S E3
               E NUCLEASE P1/CN
L2           1 S E3
               E NUCLEASE S1/CN
L3           1 S E3
               E E.C. D HIS
L4           3 S L1-L3
               E ADENOSINE/CN
L5           1 S E3
               E THMIDINE/CN
               E THYMIDINE/CN
               E THYMIDINE/CN
L6           3 S E3
               E URIDINE/CN
L7           1 S E3
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L8           1 S E3
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L9           1 S E3
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               E CYTODINE/CN
               E CYTIINE/CN
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L11          1 S E3
L12          8 S L5 OR L6 OR L7 OR L8 OR L9 OR L11

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L14          9 S L12 OR L13

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L16     111513 S L14 OR  NICOTINAMIDE# OR ADENOSINE OR CYTOSINE OR GUANOSINE O
L17        310 S L15 AND L16
L18       1304 S L15 (L) (DETN OR DETERMIN? OR ANAL? OR (ANT OR ANST)/RL)
L19        354 S L15 (L) (DETECT?)
L20       1452 S L19 OR L18
L21         68 S L20 AND L17
L22      15779 S KIT#
L23          6 S L21 AND L22

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L24          1 S E3

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Considered 04/16/04 MEC

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L26           0 S L25 AND L21
L27           0 S L19 AND L25
L28      124407 S ASSAY? OR IMMUNOASSAY?
L29           4 S L21 AND L28

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L30           1 S E3
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L31           1 S E3

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L33         321 S L*** AND L15
L34      138257 S L30 OR L31 OR L16 OR NAD OR NADH
L35         329 S L34 AND L15
L36          75 S L20 AND L35
L37           0 S L36 AND L25
L38           6 S L36 AND L28
L39           8 S L36 AND L22
L40        7031 S APOENZYM? OR APOGLYCOLATE OR TETRAZOLIUM OR DIAPHORASE
L41           2 S L40 AND L36
L42          12 S L38 OR L39 OR L41
                 SET SFIELD BI
L43        4702 S BIND? (S) EVENT?
L44           0 S L43 AND L35
                 SET SFIELD OBI
L45       33443 S RIBOFLAVIN OR PYRIDOXAL OR PYRIDOXAMINE OR PYROPHOSPHATE?
L46           4 S L45 AND L36
L47         828 S L15 (L) ACTIVIT?
L48          28 S L47 AND L34
L49           1 S L48 AND (L40 OR L43 OR L45)
L50          15 S L49 OR L46 OR L42
L51         138 S PAIR (L) LABEL?
L52           0 S L51 AND (L36 OR L47)
L53        3737 S DETECT? (L) BIND?
L54           0 S L53 AND L36
L55           4 S L53 AND L47
L56          19 S  L55 OR L50
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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 11:15:20 ON 09 DEC 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 9 Dec 2002  VOL 137 ISS 24
FILE LAST UPDATED: 8 Dec 2002  (20021208/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que l19
L3             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "NUCLEASE S1"/CN
L15         7657 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 OR NUCLEASE/OBI
L19          354 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 (L) (DETECT?/OBI)

=> d que l56
L3             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "NUCLEASE S1"/CN
L5             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ADENOSINE/CN
L6             3 SEA FILE=REGISTRY ABB=ON  PLU=ON  THYMIDINE/CN
L7             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  URIDINE/CN
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                 OR L11
L13            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  NICOTINAMIDE/CN
L14            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 OR L13
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L16       111513 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 OR  NICOTINAMIDE#/OBI OR
                 ADENOSINE/OBI OR CYTOSINE/OBI OR GUANOSINE/OBI OR THYMIDINE/OBI
                  OR URIDINE/OBI
L18         1304 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 (L) (DETN/OBI OR DETERMIN?
                 /OBI OR ANAL?/OBI OR (ANT OR ANST)/RL)
L19          354 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 (L) (DETECT?/OBI)
L20         1452 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 OR L18
L22        15779 SEA FILE=HCAPLUS ABB=ON  PLU=ON  KIT#/OBI
L28       124407 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ASSAY?/OBI OR IMMUNOASSAY?/OBI

L30            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  NAD/CN
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L31           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  NADH/CN
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                OR NADH/OBI
L35         329 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 AND L15
L36          75 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L20 AND L35
L38           6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND L28
L39           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND L22
L40        7031 SEA FILE=HCAPLUS ABB=ON  PLU=ON  APOENZYM?/OBI OR APOGLYCOLATE/
                OBI OR TETRAZOLIUM/OBI OR DIAPHORASE/OBI
L41           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L40 AND L36
L42          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 OR L39 OR L41
L43        4702 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BIND? (S) EVENT?
L45       33443 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RIBOFLAVIN/OBI OR PYRIDOXAL/OB
                I OR PYRIDOXAMINE/OBI OR PYROPHOSPHATE?/OBI
L46           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L45 AND L36
L47         828 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 (L) ACTIVIT?/OBI
L48          28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L47 AND L34
L49           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L48 AND (L40 OR L43 OR L45)
L50          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L49 OR L46 OR L42
L53        3737 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DETECT?/OBI (L) BIND?/OBI
L55           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L53 AND L47
L56          19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L55 OR L50


=> d .ca  l56 1-19

L56  ANSWER 1 OF 19  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:691401  HCAPLUS
DOCUMENT NUMBER:          137:232861
TITLE:                    Preparation of 3'-amino or 3'-amino-3'-deoxy-2'-O,4'-C-
                          methylene nucleoside analogs and oligonucleotide
                          analogs containing the nucleoside analogs and N3'-P5'
                          bond as anti-AIDS drugs
INVENTOR(S):              Imanishi, Takeshi; Kohiyori, Satoshi
PATENT ASSIGNEE(S):       Sankyo Co., Ltd., Japan
SOURCE:                   Jpn. Kokai Tokkyo Koho, 43 pp.
                          CODEN: JKXXAF
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     JP 2002255990      A2   20020911       JP 2001-352543    20011119
PRIORITY APPLN. INFO.:                   JP 2000-354326   A  20001121
OTHER SOURCE(S):          MARPAT 137:232861
GI
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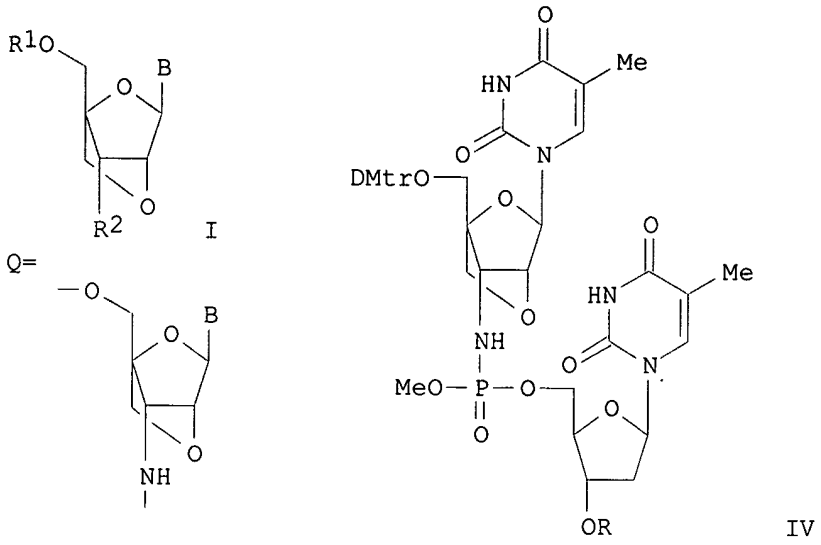

AB Bicyclo nucleoside analogs having anti-AIDS activity, oligonucleotides possessing excellent antisense or anti-gene activity and in vivo stability, and intermediates thereof are provided. 3'-Amino or 3'-azido-3'-deoxy-2'-O,4'-C-methylene nucleoside analogs [I; R1 = H, hydroxy-protecting group in nucleic acid synthesis, P(O)(OH)2 optionally protected by a protecting group in nucleic acid synthesis, P(R4a)R4b (wherein R4a, R4b = OH, SH, or NH2 optionally protected by a protecting group in nucleic acid synthesis, C1-6 alkoxy, C1-6 alkylthio, C1-7 cyanoalkoxy, C1-6 alkylamino); R2 = N3, NH2, NHR3 (wherein R3 = amino-protecting group in nucleic acid synthesis), P(O)(OH)2 optionally protected by a protecting group in nucleic acid synthesis, P(R4a)R4b (wherein R4a, R4b = same as above); B = purin-9-yl or 2-oxo-1,2-dihydropyrimidin-1-yl optionally possessing .gtoreq.1 substituent group selected from HO, SH, or NH2 protected by a protecting group in nucleic acid synthesis, C1-6 alkoxy, C1-6 alkylthio, C1-6 alkyl, and halo] and oligonucleotides contg. 1 or .gtoreq.2 nucleoside residues represented by formula Q (B = same as above) or pharmacol. acceptable salts thereof are prepd. Thus, 240 mg O,O'-bis(trimethylsilyl)thymine and 253 mg SnCl4 were added to a soln. of 300 mg 3-azido-5-O-tert-butyldiphenylsilyl-3-deoxy-4-(p-toluenesulfonyloxymethyl)-1,2-di-O-acetyl-D-ribofuranose in 6 mL 1,2-dichloroethane and stirred r for 43 h to give 91% 2'-O-acetyl-3'-azido-5'-O-tert-butyldiphenylsilyl-3'-deoxy-4'-(p-toluenesulfonyloxymethyl)-5-methyluridine which were deprotected by treatment with K2CO3 in MeOH at room temp. for 4.5 h and with Bu4NF in THF at room temp. for 1 h to give 85% 3'-azido-3'-deoxy-2'-O,4'-C-methylene-5-methyluridine (II). To a soln. of 300 mg II in 6 mL pyridine was added 415 mg 4,4'-dimethoxytrityl chloride and 12.5 mg 4-dimethylaminopyridine and stirred at room temp. for 20.5 h to give 76% 3'-azido-3'-deoxy-2'-O,4'-C-methylene-5'-O-(4,4'-dimethoxytrityl)-5-methyluridine which (110 mg) was stirred with PPh3 in pyridine at room temp. for 3.5 h to give 97% 3'-amino-3'-deoxy-2'-O,4'-C-methylene-5'-O-(4,4'-dimethoxytrityl)-5-methyluridine (III). III (10.0 mg) was condensed with 22.1 mg 3'-O-(tert-butyldimethylsilyl)thymidine 5'-(Me phosphonate) in the presence of Et3N in CCl4/MeCN at room temp. for 18 h to give 39% dinucleotide analog (IV; R = tert-butyldimethylsilyl; DMTr = 4,4'-dimethoxytrityl) which was deprotected by treatment with Bu4NF in THF to give 78% IV (R = H). To a soln. of 10.0 mg IV (R = H) and 15.5 mg diisopropylammonium tetrazolide in 0.6 mL MeCN and 0.2 mL THF was added

39.8 mg 2-cyanoethyl-N,N-diisopropylchlorophosphoramidite and stirred at room temp. for 25 h to give dinucleotide analog phosphoramidite IV [R = P(CH2CH2CN)N(iPr)2] which was used to prep. oligonucleotide analogs, e.g. 5'-TTTTTmTnTmTmTmT-3' (V; m = 5-methyl-2'-deoxycytidine, n = 3'-amino-3'-deoxy-2'-O,4'-C-methylene-5-methyluridine residue), by a Gene Assembler Plus DNA synthesizer (Pharmacia Corp.). V exhibited the formability of a triple strand (Tm = 55.degree.) with 5'-GCTAAAAAGAAAGAGAGATCG-3' and 5'-CGATCTCTCTTTCTTTTTAGC-3' better than that (Tm = 44.degree.) of natural oligonucleotide 5'-TTTTTmTTmTmTmT-3' (m = same as above).

IC ICM C07H019-06
ICS A61K031-712; A61K048-00; A61P031-18; C07H019-16; C07H021-00; C12N015-09

CC 33-9 (Carbohydrates)
Section cross-reference(s): 1

IT Anti-AIDS agents
Human immunodeficiency virus 1
(prepn. of 3'-amino or 3'-amino-3'-deoxy-2'-O,4'-C-methylene nucleoside **analogs** and **nuclease**-resistant antisense oligonucleotide **analogs** contg. them and N3'-P5' bonds as anti-AIDS drugs)

IT Nucleoside **analogs**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 3'-amino or 3'-amino-3'-deoxy-2'-O,4'-C-methylene nucleoside **analogs** and **nuclease**-resistant antisense oligonucleotide **analogs** contg. them and N3'-P5' bonds as anti-AIDS drugs)

IT Antisense oligonucleotides
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3'-amino or 3'-amino-3'-deoxy-2'-O,4'-C-methylene nucleoside **analogs** and **nuclease**-resistant antisense oligonucleotide **analogs** contg. them and N3'-P5' bonds as anti-AIDS drugs)

IT 458058-41-8 458058-42-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**assay** for resistance against **nuclease**; prepn. of 3'-amino or 3'-amino-3'-deoxy-2'-O,4'-C-methylene nucleoside **analogs** and **nuclease**-resistant antisense oligonucleotide **analogs** contg. them and N3'-P5' bonds as anti-AIDS drugs)

IT 9068-54-6, 3'-ExoNuclease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**assay** for resistance of oligodeoxynucleotides against; prepn. of 3'-amino or 3'-amino-3'-deoxy-2'-O,4'-C-methylene nucleoside **analogs** and **nuclease**-resistant antisense oligonucleotide **analogs** contg. them and N3'-P5' bonds as anti-AIDS drugs)

IT 247025-17-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 3'-amino or 3'-amino-3'-deoxy-2'-O,4'-C-methylene nucleoside **analogs** and **nuclease**-resistant antisense oligonucleotide **analogs** contg. them and N3'-P5' bonds as anti-AIDS drugs)

IT 247025-18-9P 458058-34-9P 458058-35-0P 458058-36-1P 458058-37-2P

458058-38-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3'-amino or 3'-amino-3'-deoxy-2'-O,4'-C-methylene nucleoside **analogs** and **nuclease**-resistant antisense oligonucleotide **analogs** contg. them and N3'-P5' bonds as anti-AIDS drugs)

IT 98-59-9, p-Toluenesulfonyl chloride 7288-28-0, O,O'-Bis(trimethylsilyl)thymine 14470-28-1, 4-Methoxytrityl chloride 40615-36-9, 4,4'-Dimethoxytrityl chloride 40733-27-5, 3'-O-(tert-Butyldimethylsilyl)**thymidine** 58479-61-1, tert-Butyldiphenylsilyl chloride 86030-43-5, Chlorodiisopropylaminomethoxyphosphine 89992-70-1, 2-Cyanoethyl-N,N-diisopropylchlorophosphoramidite 105931-57-5 153914-98-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of 3'-amino or 3'-amino-3'-deoxy-2'-O,4'-C-methylene nucleoside **analogs** and **nuclease**-resistant antisense oligonucleotide **analogs** contg. them and N3'-P5' bonds as anti-AIDS drugs)

IT 161790-66-5P 247025-10-1P 247025-11-2P 247025-12-3P 247025-13-4P 247025-15-6P 247025-16-7P 315665-51-1P 321882-28-4P 321882-29-5P 391259-82-8P 391259-84-0P 391259-85-1P 457659-26-6P 457659-27-7P 457659-28-8P 457659-29-9P 457659-30-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 3'-amino or 3'-amino-3'-deoxy-2'-O,4'-C-methylene nucleoside **analogs** and **nuclease**-resistant antisense oligonucleotide **analogs** contg. them and N3'-P5' bonds as anti-AIDS drugs)

IT 458058-39-4P 458058-40-7P 458619-51-7P 458619-52-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 3'-amino or 3'-amino-3'-deoxy-2'-O,4'-C-methylene nucleoside **analogs** and **nuclease**-resistant antisense oligonucleotide **analogs** contg. them and N3'-P5' bonds as anti-AIDS drugs)

L56 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:594968 HCAPLUS
DOCUMENT NUMBER: 137:151788
TITLE: Homo-doubly labeled compositions for the detection of enzyme activity in biological samples
INVENTOR(S): Packard, Beverly S.; Komoriya, Akira
PATENT ASSIGNEE(S): Oncoimmunin, Inc., USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002061038	A2	20020808	WO 2001-US49781	20011221

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-747287 A 20001222

AB The present invention provides for novel reagents whose fluorescence or absorption spectra change upon cleavage or a change in conformation of a backbone. Fluorescence or absorption spectra of these indicators change in the presence of active proteases, nucleases, glycosidases, and the like. The reagents comprise a backbone (e.g. nucleic acid, polypeptide, etc.) joining two chromophores (e.g. fluorophores) of the same species whereby the chromophores form an H-dimer resulting in quenching of the fluorescence of the fluorophores or a change in absorption spectra of the chromophores. When the backbone is cleaved or changes conformation, the chromophores are sepd., no longer forming an H-type dimer, and are de-quenched thereby providing a detectable signal. The use of a single chromophore rather than an "acceptor-donor" fluorescence resonance energy transfer system offers synthesis and performance advantages.

IC ICM C12N

CC 7-1 (Enzymes)

IT Proteins

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(nucleic acid-**binding**; homo-doubly labeled compns. for **detection** of enzyme activity in biol. samples)

IT 9001-92-7, Protease 9004-06-2, Elastase 9026-81-7, **Nuclease**

RL: ANT (Analyte); ANST (Analytical study)
(homo-doubly labeled compns. for detection of enzyme **activity** in biol. samples)

L56 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:429033 HCAPLUS

DOCUMENT NUMBER: 137:16473

TITLE: Methods and test kits for detection of a target nucleic acid by PCR using FEN nuclease to generate a signal by cleaving the DNA cleavage structure

INVENTOR(S): Sorge, Joseph A.; Whalen, Anne M.

PATENT ASSIGNEE(S): Stratagene, USA

SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044326	A2	20020606	WO 2001-US44215	20011126

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002137036	A1	20020926	US 2000-728574	20001130

PRIORITY APPLN. INFO.: US 2000-728574 A 20001130

AB The invention relates to a method of generating a signal indicative of the presence of a target nucleic acid in a sample, where the method includes forming a cleavage structure by incubating a sample comprising a target

nucleic acid with a probe having a secondary structure that changes upon binding of the probe to the target nucleic acid and further comprising a binding moiety. The invention also includes the steps of cleaving the cleavage structure with a FEN nuclease to release a nucleic acid fragment to generate a signal that is indicative of the presence of a target nucleic acid in a sample, and detecting and/or measuring the amt. of the fragment captured by binding of a binding moiety to a capture element on a solid support. PCR is used to detect the target nucleic acids using primers wherein the forward primer is located upstream of the cleavage structure and the reverse primers is located downstream of the cleavage structure. PCR simultaneously forms a cleaving structure, amplifies the target nucleic acid and cleaves the cleavage structure. FEN nuclease is thermostable and is flap-specific. The cleavage structure contains a 5' flap and an oligonucleotide primer. The secondary structure of the probe may be a stem-loop structure, a hairpin structure, an internal loop, a bulge loop, a branched structure or a pseudoknot or cloverleaf structure. The binding moiety is a nucleic acid sequence tag that binds to the capture element. The probe further comprises a label that is capable of producing a detectable signal. The cleavage structure formed comprises a pair of interactive signal generating labeled moieties (quencher and fluorescent moieties), positioned on the probe to quench the signal when the probe is not bound to the target nucleic acid. These labeled moieties are sepd. by a nuclease susceptible site, wherein the nuclease cleaves the probe to sep. the quencher and fluorescent moieties. The secondary structure of the probe is stable at or below the cleavage reaction temp., when not bound to the target nucleic acid.

IC ICM C12N

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 7

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(with secondary structure, capture element **binding** moiety in; methods and test kits for **detection** of target nucleic acid by PCR using FEN nuclease to generate signal by cleaving DNA cleavage structure)

IT 9012-90-2, DNA polymerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lacks 5' to 3' exonuclease **activity**, for amplification of target nucleic acids; methods and test kits for detection of target nucleic acid by PCR using FEN **nuclease** to generate signal by cleaving DNA cleavage structure)

L56 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	2001:868661 HCAPLUS
DOCUMENT NUMBER:	136:49292
TITLE:	Detection of RNA targets using INVADER oligonucleotide-directed cleavage reactions and construction of modified Thermus polymerase enzymes with thermostable 5'-nuclease activities
INVENTOR(S):	Allawi, Hatim; Bartholomay, Christian Tor; Chehak, Luanne; Curtis, Michelle L.; Eis, Peggy S.; Hall, Jeff G.; Ip, Hon S.; Kaiser, Michael; Kwiatkowski, Robert W., Jr.; Lukowiak, Andrew A.; Lyamichev, Victor; Ma, Wupo; Olson-munoz, Marilyn C.; Olson, Sarah M.; Schaefer, James J.; Skrzypczynski, Zbigniew; Takova, Tsetska Y.; Vedvik, Kevin L.; Lyamichev, Natalie E.; Neri, Bruce P.
PATENT ASSIGNEE(S):	Third Wave Technologies, Inc., USA
SOURCE:	PCT Int. Appl., 1266 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090337	A2	20011129	WO 2001-US17086	20010524

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-577304 A 20000524
US 2001-758282 A 20010111
US 2001-864426 A 20010524
US 2001-864636 A 20010524

AB The present invention provides novel cleavage agents and polymerases for the cleavage and modification of nucleic acid. The cleavage agents and polymerases find use, for example, for the detection and characterization of nucleic acid sequences and variations in nucleic acid sequences. In some embodiments, the 5'-nuclease activity of a variety of modified Thermus polymerase enzymes is used to cleave a target-dependent cleavage structure, thereby indicating the presence of specific nucleic acid sequences or specific variations thereof. The term "cleavage structure" refers to a structure that is formed by the interaction of at least one probe oligonucleotide (called the INVADER oligonucleotide) and a target nucleic acid, forming a structure comprising a duplex, the resulting structure being cleavable by a cleavage agent including but not limited to an enzyme. A sample suspected of contg. the target sequence is contacted with oligonucleotides capable of forming an invasive cleavage structure in the present of the target sequence and with an agent for detecting the presence of the invasive cleavage structure. ARRESTOR oligonucleotides improve sensitivity of multiple sequential invasive cleavage assays and allow use of higher concns. of primary probe without increasing background signal. The detailed description of the invention includes: (1) detection of specific nucleic acid sequences using 5'-nucleases in an INVADER-directed cleavage assay; (2) signal enhancement by incorporating the products of an invasive cleavage reaction into a subsequent invasive cleavage reaction; (3) effect of ARRESTOR oligonucleotides on signal and background in sequential invasive cleavage reactions; (4) improved enzymes for the use in INVADER oligonucleotide-directed cleavage reactions comprising RNA targets; (5) reaction design for INVADER assay detection of RNA targets; (6) kits for performing the RNA invader assay; and (7) the INVADER assay for direct detection and measurement of specific RNA analytes.

IC ICM C12N009-22
ICS C12N009-12; C12Q001-68
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 7

L56 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:634531 HCAPLUS
DOCUMENT NUMBER: 136:258038
TITLE: Analysis of the chromosome sequence of the legume

symbiont Sinorhizobium meliloti strain 1021

AUTHOR(S): Capela, Delphine; Barloy-Hubler, Frederique; Gouzy, Jerome; Bothe, Gordana; Ampe, Frederic; Batut, Jacques; Boistard, Pierre; Becker, Anke; Boutry, Marc; Cadieu, Edouard; Dreano, Stephane; Gloux, Stephanie; Godrie, Therese; Goffeau, Andre; Kahn, Daniel; Kiss, Erno; Lelaure, Valerie; Masuy, David; Pohl, Thomas; Portetelle, Daniel; Puhler, Alfred; Purnelle, Benedicte; Ramsperger, Ulf; Renard, Clotilde; Thebault, Patricia; Vandenbol, Micheline; Weidner, Stefan; Galibert, Francis

CORPORATE SOURCE: Laboratoire de Biologie Moleculaire des Relations Plantes-Microorganismes, Unite Mixte de Recherche (UMR) 215 Centre National de la Recherche Scientifique (CNRS), Institut National de la Recherche Agronomique, Chemin, Tolosan, F-31326, Fr.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(17), 9877-9882
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sinorhizobium meliloti is an .alpha.-proteobacterium that forms agronomically important N2-fixing root nodules in legumes. We report here the complete sequence of the largest constituent of its genome, a 62.7% GC-rich 3654,135-bp circular chromosome. Annotation allowed assignment of a function to 59% of the 3341 predicted protein-coding ORFs, the rest exhibiting partial, weak, or no similarity with any known sequence. Unexpectedly, the level of reiteration within this replicon is low, with only two genes duplicated with more than 90% nucleotide sequence identity, transposon elements accounting for 2.2% of the sequence, and a few hundred short repeated palindromic motifs (RIME1, RIME2, and C) widespread over the chromosome. Three regions with a significantly lower GC content are most likely of external origin. Detailed annotation revealed that this replicon contains all housekeeping genes except two essential genes that are located on pSymB. Amino acid/peptide transport and degrdn. and sugar metab. appear as two major features of the S. meliloti chromosome. The presence in this replicon of a large no. of nucleotide cyclases with a peculiar structure, as well as of genes homologous to virulence determinants of animal and plant pathogens, opens perspectives in the study of this bacterium both as a free-living soil microorganism and as a plant symbiont.

CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 6, 10

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:185964 HCAPLUS

DOCUMENT NUMBER: 134:221001

TITLE: Mutant of RAD51 gene and its use in the diagnosis of predisposition to breast cancer

INVENTOR(S): Wang, Wendy Weiching; Struewing, Jeffrey P.

PATENT ASSIGNEE(S): The Government of the United States of America as Represented by the Secreta, USA

SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001018254	A2	20010315	WO 2000-US24786	20000908

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000073646	A5	20010410	AU 2000-73646	20000908
PRIORITY APPLN. INFO.:			US 1999-153288P	P 19990910
			WO 2000-US24786	W 20000908

AB The present invention describes the identification of a mutant of the RAD51 gene. The mutant is assocd. with an increase in the risk of developing breast cancer in women who carry a BRCA1 or BRCA2 mutation. The mutant consists of three genetic variants: a guanine to cytosine (G-135.fwdarw.C) transversion at nucleotide position 135 in the 5' untranslated region of the RAD51 gene, a guanine to thymine (G-2339.fwdarw.T) transversion at nucleotide position minus (-) 2339 upstream (5') from the transcription start site of the RAD51 gene, and a deletion of two adenine residues beginning at nucleotide position minus (-) 3189 upstream (5') from the transcription start site of the RAD51 gene. The thus methods for diagnosing genetic predisposition or susceptibility to breast cancer in a subject.

IC ICM C12Q001-68
ICS C07K014-47

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3, 6

IT Test **kits**
(diagnostic; mutant of RAD51 gene and use in diagnosis of predisposition to breast cancer)

IT 9075-08-5, **Nuclease**, restriction endodeoxyribo-
RL: ARG (Analytical reagent use); **ANST (Analytical study)**; USES (Uses)
(for gene RAD51 mutation **detection**; mutant of RAD51 gene and use in diagnosis of predisposition to breast cancer)

IT **71-30-7, Cytosine**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(transversion from guanine at position of -2339 in gene RAD51; mutant of RAD51 gene and use in diagnosis of predisposition to breast cancer)

L56 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	2001:50852 HCAPLUS
DOCUMENT NUMBER:	134:111217
TITLE:	Identification of polymorphisms within vascular endothelial growth factor (VEGF) gene and genotyping method for diagnosis application
INVENTOR(S):	Brenchley, Paul Ernest Charles; Watson, Carolyn
PATENT ASSIGNEE(S):	Victoria University of Manchester, UK
SOURCE:	PCT Int. Appl., 50 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004351	A2	20010118	WO 2000-GB2430	20000706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1200621	A2	20020502	EP 2000-942213	20000706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: GB 1999-15978 A 19990708
GB 1999-21801 A 19990916
WO 2000-GB2430 W 20000706

AB The present invention relates to an in vitro method for diagnosing or detecting a predisposition to a disease or disorder assocd. with abnormal VEGF gene expression and kits for use in such a method. The method comprises examg. regulatory elements assocd. with the VEGF gene to detect the presence of a genetic polymorphism which is linked to the disease or disorder. Specifically, the invention identified 18 sequence polymorphism in the promoter and exon 1 region of VEGF gene using single-stranded conformation (SSCP) polymorphism anal. and direct PCR-sequencing. The most two common ones (G+405.fwdarw.C and C-460.fwdarw.T) are examd. for their allelic frequency in various diseases and linked to diseases with abnormal VEGF gene expression such as ischemic heart disease, nephrotic syndrome, inflammatory joint disorder, rheumatoid arthritis, ovarian carcinoma, diabetes, and proteinuria. A PCR-RFLP typing system and its diagnostic kit is developed which include PCR primers, restriction endonucleases, DNA extn. buffers, agarose gel loading buffer and electrophoresis running buffers.

IC ICM C12Q001-68

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 9, 14

IT Test **kits**
(diagnostic; identification of polymorphisms within vascular endothelial growth factor (VEGF) gene and genotyping method for diagnosis application)

IT 9075-08-5, **Nuclease**, restriction endodeoxyribo- 86352-29-6, Restriction endonuclease BstUI 160995-57-3, Restriction endonuclease BsmFI
RL: ARG (Analytical reagent use); **ANST (Analytical study)**; USES (Uses)
(identification of polymorphisms within vascular endothelial growth factor (VEGF) gene and genotyping method for diagnosis application)

IT **71-30-7, Cytosine**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(substituted to T at -460 or for G at +405 of VEGF gene; identification of polymorphisms within vascular endothelial growth factor (VEGF) gene and genotyping method for diagnosis application)

L56 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:790667 HCAPLUS
DOCUMENT NUMBER: 133:345539

TITLE: Diagnostic sequencing of nucleic acids by a combination of specific cleavage and mass spectrometry
INVENTOR(S): Zabeau, Marc; Stanssens, Patrick
PATENT ASSIGNEE(S): Methexis N.V., Belg.
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066771	A2	20001109	WO 2000-EP3904	20000430
WO 2000066771	A3	20010208		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1173622	A2	20020123	EP 2000-940234	20000430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001005293	A	20011220	NO 2001-5293	20011029

PRIORITY APPLN. INFO.: US 1999-131984P P 19990430
WO 2000-EP3904 W 20000430

AB The present invention is in the field of nucleic acid-based diagnostic assays. More particularly, it relates to methods useful for the diagnostic sequencing of regions of sample nucleic acids for which a prototypic or ref. sequence is already available (also referred to as re-sequencing), or which may be detd. using the methods described herein. This diagnostic technol. is useful in areas that require such re-sequencing in a rapid and reliable way including: the identification of the various allelic sequences of a certain region/gene; the scoring of disease-assocd. mutations; the detection of somatic variations; studies in the field of mol. evolution; the detn. of the nucleic acid sequences of prokaryotic and eukaryotic genomes; identifying one or more nucleic acids in one or more biol. samples; and detg. the expression profile of genes in a biol. sample and other areas.

IC ICM C12Q001-68
CC 3-1 (Biochemical Genetics)
IT Test **kits**
(for DNA sequencing; diagnostic sequencing of nucleic acids by combination of specific cleavage and mass spectrometry)
IT 9001-99-4, RNase 9025-82-5, Phosphodiesterase 9026-12-4, RNase T1 9055-11-2, Endonuclease 9075-08-5, Restriction endonuclease 37205-57-5, RNase U2 37228-74-3, Exonuclease 54576-84-0, **Nuclease** P1 73508-01-7, **Cytosine**-specific ribonuclease 157972-11-7, Cusativin 305362-62-3, RNase phyM
RL: ARU (Analytical role, unclassified); CAT (Catalyst use); **ANST (Analytical study)**; USES (Uses)
(cleavage of nucleic acids with, for sequencing; diagnostic sequencing of nucleic acids by combination of specific cleavage and mass spectrometry)

L56 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:679263 HCAPLUS
DOCUMENT NUMBER: 134:188814
TITLE: Re-annotating the Mycoplasma pneumoniae genome sequence: adding value, function and reading frames
AUTHOR(S): Dandekar, Thomas; Huynen, Martijn; Regula, Jorg Thomas; Ueberle, Barbara; Zimmermann, Carl Ulrich; Andrade, Miguel A.; Doerks, Tobias; Sanchez-Pulido, Luis; Snel, Berend; Suyama, Mikita; Yuan, Yan P.; Herrmann, Richard; Bork, Peer
CORPORATE SOURCE: EMBL, Heidelberg, D-69012, Germany
SOURCE: Nucleic Acids Research (2000), 28(17), 3278-3288
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Four years after the original sequence submission, we have re-annotated the genome of Mycoplasma pneumoniae to incorporate novel data. The total no. of ORFss has been increased from 677 to 688 (10 new proteins were predicted in intergenic regions, two further were newly identified by mass spectrometry and one protein ORF was dismissed) and the no. of RNAs from 39 to 42 genes. For 19 of the now 35 tRNAs and for six other functional RNAs the exact genome positions were re-annotated and two new tRNALeu and a small 200 nt RNA were identified. Sixteen protein reading frames were extended and eight shortened. For each ORF a consistent annotation vocabulary has been introduced. Annotation reasoning, annotation categories and comparisons to other published data on M. pneumoniae functional assignments are given. Exptl. evidence includes 2-dimensional gel electrophoresis in combination with mass spectrometry as well as gene expression data from this study. Compared to the original annotation, we increased the no. of proteins with predicted functional features from 349 to 458. The increase includes 36 new predictions and 73 protein assignments confirmed by the published literature. Furthermore, there are 23 redns. and 30 addns. with respect to the previous annotation. MRNA expression data support transcription of 184 of the functionally unassigned reading frames.

CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 6, 7, 10

IT 9023-35-2, Pseudouridylate synthase 9023-83-0, Ribose 5-phosphate isomerase 9025-82-5, Phosphodiesterase 9026-37-3 9026-99-7, Phosphopantetheine adenylyltransferase 9027-41-2, Hydrolase 9027-80-9, Adenine phosphoribosyltransferase 9029-83-8, Serine hydroxymethyltransferase 9030-24-4, Uracil phosphoribosyltransferase 9031-50-9, Nucleotidyl transferase 9032-82-0 9033-07-2, Glycosyltransferase 9033-25-4, Methyltransferase 9075-08-5, Restriction endonuclease 9079-67-8, **NADH**-oxidoreductase 37217-33-7, DNA polymerase III 37278-30-1, Holo-acyl-carrier protein synthase 37288-21-4, Acyl carrier protein phosphodiesterase 37288-24-7, 3'-5' Exoribonuclease 39369-30-7, RRNA methylase 39433-98-2, Galactose-6-phosphate isomerase 52232-48-1, Glutamyl-tRNAgln amidotransferase 57657-66-6, Dihydroxyacetone kinase 70457-12-4, PpGpp 3'-pyrophosphohydrolase 123609-48-3, Deoxyribose-phosphate aldolase (MPN63) (Mycoplasma pneumoniae strain M129 gene deoC) 132052-98-3, DNA gyrase (MPN003) (Mycoplasma pneumoniae strain M129 gene gyrB subunit B) 135847-88-0, Adhesin-related protein, 30,000-dalton (MPN453) (Mycoplasma pneumoniae strain M129 gene H08-orf274) 147301-96-0, Cytadherence accessory protein (MPN452) (Mycoplasma pneumoniae strain M129 gene hmw3) 165040-72-2, Protein MPN309 (Mycoplasma pneumoniae strain M129 gene P65) 174632-18-9, UDP-galactopyranose mutase 174957-83-6, Synthetase, **adenosine** triphosphate (Mycoplasma pneumoniae strain M129 gene atpI subunit I) 174957-84-7 174957-85-8, Synthetase, **adenosine**

triphosphate (Mycoplasma pneumoniae strain M129 gene atpE subunit c) 174957-86-9, Synthetase, **adenosine** triphosphate (Mycoplasma pneumoniae strain M129 gene atpF subunit b) 174957-87-0, Synthetase, **adenosine** triphosphate (Mycoplasma pneumoniae strain M129 gene atpH subunit .delta.) 174957-88-1, Synthetase, **adenosine** triphosphate (Mycoplasma pneumoniae strain M129 gene atpA subunit .alpha.) 174957-89-2, Synthetase, **adenosine** triphosphate (Mycoplasma pneumoniae strain M129 gene atpG subunit .gamma.) 174957-90-5, Synthetase, **adenosine** triphosphate (Mycoplasma pneumoniae strain M129 gene atpD subunit .beta.) 174957-91-6, Synthetase, **adenosine** triphosphate (Mycoplasma pneumoniae strain M129 gene atpC subunit .epsilon.) 174957-92-7, Protein (Mycoplasma pneumoniae strain M129 569-amino acid) 174957-93-8, Isomerase, galactose 6-phosphate (Mycoplasma pneumoniae strain M129 gene lacA subunit) 174957-94-9, Protein MPN593 (Mycoplasma pneumoniae strain M129 gene D02-orf122b) 174957-95-0, Protein MPN592 (Mycoplasma pneumoniae strain M129 gene D02-orf521) 174957-96-1, Protein MPN591 (Mycoplasma pneumoniae strain M129 gene D02-orf353V) 174957-97-2, Protein MPN590 (Mycoplasma pneumoniae strain M129 gene D02-orf217L) 174957-98-3, Protein MPN589 (Mycoplasma pneumoniae strain M129 gene D02-orf157L) 174957-99-4 174958-00-0, Protein MPN203 (Mycoplasma pneumoniae strain M129 gene GT9-orf127) 174958-02-2, Protein MPN202 (Mycoplasma pneumoniae strain M129 gene GT9-orf313) 174958-03-3, Protein MPN201 (Mycoplasma pneumoniae strain M129 gene GT9-orf238) 174958-04-4, Protein MPN200 (Mycoplasma pneumoniae strain M129 gene GT9-orf798) 174958-05-5, Protein MPN199 (Mycoplasma pneumoniae strain M129 gene GT9-orf760) 174958-06-6, Adenine-specific methyltransferase EcoRI (MPN198) (Mycoplasma pneumoniae strain M129 gene mte1) 174958-07-7, Oligoendopeptidase F (MPN197) (Mycoplasma pneumoniae strain M129 gene pepF) 174958-08-8, Pseudouridylate synthase I (MPN196) (Mycoplasma pneumoniae strain M129 gene hisT) 174958-09-9, Cobalt transporter membrane protein-like protein MPN195 (Mycoplasma pneumoniae strain M129 gene GT9-orf434) 174958-10-2, Cobalt transporter ATP-binding protein-like protein MPN184 (Mycoplasma pneumoniae strain M129 gene hisP) 174958-11-3, Cobalt transporter ATP-binding protein-like protein MPN193 (Mycoplasma pneumoniae strain M129 gene cysA) 174958-12-4, Ribosomal protein L17 (MPN192) (Mycoplasma pneumoniae strain M129 gene rplQ) 174958-13-5, RNA polymerase MPN191 (Mycoplasma pneumoniae strain M129 gene rpoA .alpha.-core-subunit) 174958-14-6, Ribosomal protein S11 (MPN190) (Mycoplasma pneumoniae strain M129 gene rpsK) 174958-15-7, Ribosomal protein S13 (MPN189) (Mycoplasma pneumoniae strain M129 gene rpsM) 174958-16-8, Initiation factor 1 (MPN187) (Mycoplasma pneumoniae strain M129 gene infA) 174958-17-9, Methionine amino peptidase MPN186 (Mycoplasma pneumoniae strain M129 gene map) 174958-18-0, Adenylate kinase MPN185 (Mycoplasma pneumoniae strain M129 gene adk) 174958-19-1, Preprotein translocase MPN184 (Mycoplasma pneumoniae strain M129 gene secY subunit) 174958-20-4, Ribosomal protein L15 (MPN183) (Mycoplasma pneumoniae strain M129 gene rplO) 174958-21-5 174958-22-6, Ribosomal protein L18 (MPN181) (Mycoplasma pneumoniae strain M129 gene rplR) 174958-23-7, Ribosomal protein L6 (MPN180) (Mycoplasma pneumoniae strain M129 gene rplF) 174958-24-8, Ribosomal protein S8 (MPN179) (Mycoplasma pneumoniae strain M129 gene rpsH) 174958-25-9, Ribosomal protein L5 (MPN177) (Mycoplasma pneumoniae strain M129 gene rplE) 174958-26-0, Ribosomal protein L24 (MPN176) (Mycoplasma pneumoniae strain M129 gene rplX) 174958-27-1, Ribosomal protein L14 (MPN175) (Mycoplasma pneumoniae strain M129 gene rplN) 174958-28-2, Ribosomal protein S17 (MPN174) (Mycoplasma pneumoniae strain M129 gene rpsQ) 174958-29-3, Ribosomal protein L29 (MPN173) (Mycoplasma pneumoniae strain M129 gene rpmC) 174958-31-7 174958-32-8 174958-33-9, ParA family ATPase chromosome partition protein MPN688 (Mycoplasma pneumoniae strain M129 gene soj) 174958-34-0, Protein MPN687 (Mycoplasma pneumoniae strain

M129 gene K05-orf250) 174958-35-1, Chromosomal replication initiator protein DnaA (MPN686) (Mycoplasma pneumoniae strain M129 gene dnaA) 174958-36-2, Sulfate transporter MPN685 (Mycoplasma pneumoniae strain M129 gene cysA) 175010-17-0 175010-27-2, Ribosomal protein S14 (MPN178) (Mycoplasma pneumoniae strain M129 gene rpsN) 178807-84-6, Competence locus operon protein 3-like protein MPN451 (Mycoplasma pneumoniae strain M129 gene come3) 178807-85-7, Protein MPN450 (Mycoplasma pneumoniae strain M129 gene orf7) 178807-88-0, Cytadherence accessory protein HMW1 (MPN447) (Mycoplasma pneumoniae strain M129 gene hmw1) 178807-89-1, Ribosomal protein S4 (MPN446) (Mycoplasma pneumoniae strain M129 gene rpsD) 183398-76-7, GenBank AE000033 183398-77-8, GenBank AE000034 183398-78-9, GenBank AE000035 183398-79-0, GenBank AE000036 183398-80-3, GenBank AE000037 183398-81-4, GenBank AE000038 183398-82-5, GenBank AE000039 183398-83-6, GenBank AE000040 183398-84-7, GenBank AE000041 183398-85-8, GenBank AE000042 183398-86-9, GenBank AE000043 183398-87-0, GenBank AE000044 183398-88-1, GenBank AE000045 183398-89-2, GenBank AE000046 183398-90-5, GenBank AE000047 183398-91-6, GenBank AE000048 183398-92-7, GenBank AE000049 183398-93-8, GenBank AE000050 183398-94-9, GenBank AE000051 183398-95-0, GenBank AE000052 183398-96-1, GenBank AE000053 183398-97-2, GenBank AE000054 183398-98-3, GenBank AE000055 183398-99-4, GenBank AE000056 183399-00-0, GenBank AE000057 183399-01-1, GenBank AE000058 183399-12-4, GenBank AE000001 183399-13-5, GenBank AE000002 183399-14-6, GenBank AE000003 183399-15-7, GenBank AE000004 183399-16-8, GenBank AE000005 183399-17-9, GenBank AE000006 183399-18-0, GenBank AE000007 183399-19-1, GenBank AE000008 183399-20-4, GenBank AE000009 183399-21-5, GenBank AE000010 183399-22-6, GenBank AE000011 183399-23-7, GenBank AE000012 183399-24-8, GenBank AE000013 183399-25-9, GenBank AE000014 183399-26-0, GenBank AE000015 183399-27-1, GenBank AE000016 183399-28-2, GenBank AE000017 183399-29-3, GenBank AE000018 183399-30-6, GenBank AE000019 183399-31-7, GenBank AE000020 183399-32-8, GenBank AE000021 183399-33-9, GenBank AE000022 183399-34-0, GenBank AE000023 183399-35-1, GenBank AE000024 183399-36-2, GenBank AE000025 183399-37-3, GenBank AE000026 183399-38-4, GenBank AE000027 183399-39-5, GenBank AE000028 183399-40-8, GenBank AE000029 183399-41-9, GenBank AE000030 183399-42-0, GenBank AE000031 183399-43-1, GenBank AE000032 183399-56-6, GenBank AE000059 183399-57-7, GenBank AE000060 183399-58-8, GenBank AE000061 183399-59-9, GenBank AE000062 183399-60-2, GenBank AE000063 184491-71-2, Protein MG153 (MPN153) (Mycoplasma pneumoniae strain M129 gene E07-orf1113) 184491-75-6, Protein MPN152 (Mycoplasma pneumoniae strain M129 gene E07-orf794) 184491-76-7, Protein MPN151 (Mycoplasma pneumoniae strain M129 gene E07-orf133) 184491-77-8, Protein MPN150 (Mycoplasma pneumoniae strain M129 gene E07-orf224) 184491-78-9, Protein MPN149 (Mycoplasma pneumoniae strain M129 gene E07-orf434) 184491-80-3, Protein MPN148 (Mycoplasma pneumoniae strain M129 gene E07-orf140) 184491-81-4, Protein MPN147 (Mycoplasma pneumoniae strain M129 gene E07-orf485) 184491-82-5, Protein MPN146 (Mycoplasma pneumoniae strain M129 gene E07-orf265) 184491-83-6, Protein MPN145 (Mycoplasma pneumoniae strain M129 gene E07-orf179) 184491-84-7, Protein MPN144 (Mycoplasma pneumoniae strain M129 gene E07-orf413) 184491-85-8, Protein MPN143 (Mycoplasma pneumoniae strain M129 gene E07-orf175) 184491-86-9, Cytadherence-associated protein MPN142 (Mycoplasma pneumoniae strain M129 gene orf6) 184491-87-0, ADP1-MYCPN adhesin P1 MPN141 (Mycoplasma pneumoniae strain M129 gene P1) 184491-92-7, Protein MPN139 (Mycoplasma pneumoniae strain M129 gene E07-orf163) 184491-93-8, Protein MPN138 (Mycoplasma pneumoniae strain M129 gene E07-orf166) 184491-94-9, Protein (MPN137) (Mycoplasma

pneumoniae strain M129 gene E07-orf228) 184491-95-0, Sn-glycerol-3-phosphate transport system permease protein (MPN136) (Mycoplasma pneumoniae strain M129 gene ugpE) 184491-96-1, Sn-glycerol-3-phosphate transport system permease protein (MPN135) (Mycoplasma pneumoniae strain M129 gene ugpA) 184491-97-2, Sn-glycerol-3-phosphate transport system permease protein (MPN134) (Mycoplasma pneumoniae strain M129 gene ugpC) 184491-98-3, Lipoprotein MG186 (MPN133) (Mycoplasma pneumoniae strain M129 gene E07-orf301) 184491-99-4, Protein MPN132 (Mycoplasma pneumoniae strain M129 gene E07-orf256L) 184492-01-1, Protein MPN131 (Mycoplasma pneumoniae strain M129 gene E07-orf221V) 184492-04-4, Protein MPN130 (Mycoplasma pneumoniae strain M129 gene C09-orf140o) 184492-05-5, Adhesin P1 (MPN129) (Mycoplasma pneumoniae strain M129 gene C09-orf149b) 184492-06-6, Protein MPN128 (Mycoplasma pneumoniae strain M129 gene C09-orf149a) 184492-07-7, Protein MPN127 (Mycoplasma pneumoniae strain M129 gene C09-orf180) 184492-08-8, Protein MG207 (MPN126) (Mycoplasma pneumoniae strain M129 gene C09-orf159) 184492-09-9, Excinuclease ABC (MPN125) (Mycoplasma pneumoniae strain M129 gene uvrC subunit C) 184492-10-2, Protein MPN124 (Mycoplasma pneumoniae strain M129 gene yqxE) 184492-11-3, Topoisomerase IV (MPN123) (Mycoplasma pneumoniae strain M129 gene parC subunit A) 184492-12-4, Topoisomerase IV (MPN122) (Mycoplasma pneumoniae strain M129 gene parB subunit B) 184492-13-5, Protein MPN121 (Mycoplasma pneumoniae strain M129 gene C09-orf121) 184492-14-6, Protein MPN120 (Mycoplasma pneumoniae strain M129 gene C09-orf217) 184492-15-7, Protein MPN119 (Mycoplasma pneumoniae strain M129 gene C09-orf910) 184492-16-8 184492-17-9, Protein formation initiation factor IF-3 (Mycoplasma pneumoniae strain M129 gene infC) 184492-18-0, Acyltransferase MPN114 (Mycoplasma pneumoniae strain M129 gene cpt2) 184492-19-1, Permease MPN112 (Mycoplasma pneumoniae strain M129 gene C09-orf130b) 184492-20-4, G3P Transporter-like protein MPN113 (Mycoplasma pneumoniae strain M129 gene C09-orf223) 184492-21-5, Protein MPN111 (Mycoplasma pneumoniae strain M129 gene C09-orf422) 184492-22-6, Protein MPN110 (Mycoplasma pneumoniae strain M129 gene C09-orf718) 184492-23-7, Protein MPN109 (Mycoplasma pneumoniae strain M129 gene C09-orf165) 184538-71-4 184656-48-2, Protein MPN108 (Mycoplasma pneumoniae strain M129 gene C09-orf404) 184656-49-3, Protein MPN107 (Mycoplasma pneumoniae strain M129 gene C09-orf251) 184656-50-6, Phenylalanyl-tRNA synthetase MPN106 (Mycoplasma pneumoniae strain M129 gene pheT .beta.-chain) 184656-51-7, Phenylalanyl-tRNA synthetase MPN105 (Mycoplasma pneumoniae strain M129 gene pheS .alpha.-subunit) 184656-52-8, Protein MPN104 (Mycoplasma pneumoniae strain M129 gene C09-orf104) 184656-53-9, Protein MPN103 (Mycoplasma pneumoniae strain M129 gene C09-orf172) 184656-54-0, Cytadherence-associated protein MPN102 (Mycoplasma pneumoniae strain M129 gene C09-orf272) 184656-55-1, Protein MPN101 (Mycoplasma pneumoniae strain M129 gene C09-orf428V) 184656-56-2, Amino acid transporter MPN095 (Mycoplasma pneumoniae strain M129 gene R02-orf254) 184656-57-3, Protein MPN099 (Mycoplasma pneumoniae strain M129 gene R02-orf347L) 184656-58-4, Protein MPN098 (Mycoplasma pneumoniae strain M129 gene R02-orf147) 184656-59-5, Protein MPN097 (Mycoplasma pneumoniae strain M129 gene R02-orf541) 184656-60-8, Amino acid transporter MPN096 (Mycoplasma pneumoniae strain M129 gene R02-orf264) 184656-61-9, Protein MPN94 (Mycoplasma pneumoniae strain M129 gene R02-orf140) 184656-62-0, Cytadherence-associated protein MPN93 (Mycoplasma pneumoniae strain M129 gene R02-orf301) 184656-63-1, Cytadherence-associated protein MPN92 (Mycoplasma pneumoniae strain M129 gene R02-orf173) 184656-64-2, Protein MPN91 (Mycoplasma pneumoniae strain M129 gene R02-orf138) 184656-65-3, Adhesin P1 (MPN90) (Mycoplasma pneumoniae strain M129 gene R02-orf329) 184656-69-7, Protein MPN88 (Mycoplasma pneumoniae strain M129 gene R02-orf101) 184656-70-0, Protein MPN89 (Mycoplasma pneumoniae strain M129 gene hsdS) 184656-76-6, Adhesin

P1 (MPN87) (Mycoplasma pneumoniae strain M129 gene R02-orf150) 184656-77-7, Adhesin P1 (MPN86) (Mycoplasma pneumoniae strain M129 gene R02-orf105) 184656-78-8, Adhesin P1 (MPN85) (Mycoplasma pneumoniae strain M129 gene R02-orf440) 184656-79-9, Protein MPN84 (Mycoplasma pneumoniae strain M129 gene R02-orf524) 184656-80-2, Protein MPN83 (Mycoplasma pneumoniae strain M129 gene R02-orf533) 184656-81-3, Transketolase (MPN82) (Mycoplasma pneumoniae strain M129 gene tklB isoenzyme 1) 184656-82-4, Glutamine transporter (MPN81) (Mycoplasma pneumoniae strain M129 gene glnQ) 184656-83-5, ABC (ATP-binding cassette-containing) transport protein (MPN80) (Mycoplasma pneumoniae strain M129 gene R02-orf1386V subunit) 184656-84-6, 1-Phosphofructokinase (MPN79) (Mycoplasma pneumoniae strain M129 gene fruK) 184656-85-7, Fructose-permease IIBC component (MPN78) (Mycoplasma pneumoniae strain M129 gene fruA) 184656-87-9, Protein MPN76 (Mycoplasma pneumoniae strain M129 gene uhpT) 184656-88-0, Glycosyltransferase (MPN75) (Mycoplasma pneumoniae strain M129 gene ywdF) 184656-89-1, Protein MPN74 (Mycoplasma pneumoniae strain M129 gene D09-orf147) 184656-90-4, Phosphoribosylpyrophosphate synthetase (MPN73) (Mycoplasma pneumoniae strain M129 gene prs) 184656-91-5, Nucelotidyl transferase/polynucleotide cleavage-like protein MPN72 (Mycoplasma pneumoniae strain M129 gene yabF) 184656-92-6, Protein MPN71 (Mycoplasma pneumoniae strain M129 gene yabC) 184656-93-7, Protein MPN70 (Mycoplasma pneumoniae strain M129 gene D09-orf127a) 184657-03-2, Protein MPN68 (Mycoplasma pneumoniae strain M129 gene SecE) 184657-04-3, Transcription antitermination factor (MPN67) (Mycoplasma pneumoniae strain M129 gene nusG) 184657-05-4, Phosphomannomutase/phosphoglucomutase-like protein MPN66 (Mycoplasma pneumoniae strain M129 gene cpsG) 184657-06-5, Cytidine deaminase (MPN65) (Mycoplasma pneumoniae strain M129 gene cdd) 184657-07-6, **Thymidine** phosphorylase (MPN64) (Mycoplasma pneumoniae strain M129 gene deoA) 184657-08-7, Purine-nucleoside phosphorylase (MPN62) (Mycoplasma pneumoniae strain M129 gene deoD) 184657-09-8, Signal recognition particle protein (MPN61) (Mycoplasma pneumoniae strain M129 gene ffh)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(re-annotating Mycoplasma pneumoniae genome sequence: adding value, function and reading frames)

IT 184657-10-1, S-Adenosylmethionine synthetase (MPN60) (Mycoplasma pneumoniae strain M129 gene metX isoenzyme 2) 184657-11-2, o-Sialoglycoprotein endopeptidase (MPN59) (Mycoplasma pneumoniae strain M129 gene gcp) 184657-12-3, Protein MPN58 (Mycoplasma pneumoniae strain M129 gene D09-orf485) 184657-13-4, Spermidine/putrescine transporter (MPN57) (Mycoplasma pneumoniae strain M129 gene potI) 184657-14-5, Spermidine/putrescine transporter (MPN56) (Mycoplasma pneumoniae strain M129 gene potB) 184657-15-6, Spermidine/putrescine transporter (MPN55) (Mycoplasma pneumoniae strain M129 gene potA) 184657-16-7, Phosphocarrier protein HPr MPN53 (Mycoplasma pneumoniae strain M129 gene ptsH) 184657-17-8, Lipoprotein MPN52 (Mycoplasma pneumoniae strain M129 gene D09-orf657) 184657-18-9, Glycerol-3-phospate dehydrogenase (MPN51) (Mycoplasma pneumoniae strain M129 gene glpD) 184657-19-0, Glycerol kinase (MPN50) (Mycoplasma pneumoniae strain M129 gene glpK) 184657-20-3, Membrane export protein MPN49 (Mycoplasma pneumoniae strain M129 gene D09-orf632) 184657-21-4, Protein MPN54 (Mycoplasma pneumoniae strain M129 gene D09-orf123) 184657-22-5, Membrane export protein MPN048 (Mycoplasma pneumoniae strain M129 gene D09-orf518) 184657-23-6, Nicotinate phosphoribosyl transferase-like protein MPN047 (Mycoplasma pneumoniae strain M129 gene D09-orf451) 184657-24-7, Aspartyl-tRNA synthetase (MPN046) (Mycoplasma pneumoniae strain M129 gene aspS) 184657-25-8, Histidyl-tRNA synthetase (MPN045) (Mycoplasma pneumoniae strain M129 gene hisS) 184657-26-9, **Thymidine** kinase (MPN044)

(Mycoplasma pneumoniae strain M129 gene tdk) 184657-28-1, Glycerol uptake facilitator MPN043 (Mycoplasma pneumoniae strain M129 gene glpF) 184657-29-2, Protein MPN042 (Mycoplasma pneumoniae strain M129 gene B01-orf672) 184657-31-6, DNA polymerase III (dnaE) MPN034 (Mycoplasma pneumoniae strain M129 gene polC .alpha.-chain) 184657-32-7, Protein MPN041 (Mycoplasma pneumoniae strain M129 gene B01-orf186L) 184657-33-8, Protein MPN040 (Mycoplasma pneumoniae strain M129 gene B01-orf103b) 184657-34-9, Protein MPN039 (Mycoplasma pneumoniae strain M129 gene B01-orf338) 184657-35-0, Protein MPN038 (Mycoplasma pneumoniae strain M129 gene B01-orf116L) 184657-36-1, Protein MPN037 (Mycoplasma pneumoniae strain M129 gene B01-orf147) 184657-37-2, Protein MPN036 (Mycoplasma pneumoniae strain M129 gene B01-orf673) 184657-38-3, Protein MPN035 (Mycoplasma pneumoniae strain M129 gene B01-orf666) 184657-39-4, Phosphoribosyltransferase, uracil (Mycoplasma pneumoniae strain M129 gene upp) 184657-40-7, Hydrolase (MPN032) (Mycoplasma pneumoniae strain M129 gene B01-orf108) 184657-41-8, Protein MPN031 (Mycoplasma pneumoniae strain M129 gene B01-orf203) 184657-42-9, Protein MPN030 (Mycoplasma pneumoniae strain M129 gene B01-orf168) 184657-43-0, Elongation factor P MPN029 (Mycoplasma pneumoniae strain M129 gene efp) 184657-44-1, Sugar transferase MPN028 (Mycoplasma pneumoniae strain M129 gene trsB) 184657-45-2, Protein MPN027 (Mycoplasma pneumoniae strain M129 gene B01-orf274) 184657-46-3, GTPase-like protein MPN026 (Mycoplasma pneumoniae strain M129 gene yyaF) 184657-47-4, Fructose-bisphosphate aldolase MPN025 (Mycoplasma pneumoniae strain M129 gene tsr) 184657-48-5, DNA-directed RNA polymerase MPN024 (Mycoplasma pneumoniae strain M129 gene rpoE .delta.-subunit) 184657-49-6, Methionyl-tRNA synthetase MPN023 (Mycoplasma pneumoniae strain M129 gene metS) 184657-50-9, Proline iminopeptidase MPN022 (Mycoplasma pneumoniae strain M129 gene pip) 184657-51-0, Heat shock protein DnaJ (MPN021) (Mycoplasma pneumoniae strain M129 gene dnaJ) 184657-52-1, Helicase-like pretein MPN020 (Mycoplasma pneumoniae strain M129 gene yb95) 184657-53-2, ATP-binding transporter MPN019 (Mycoplasma pneumoniae strain M129 gene msbA) 184657-54-3, ATP-binding transporter MPN018 (Mycoplasma pneumoniae strain M129 gene pmd1) 184657-56-5, 5,10-Methylene-tetrahydrofolate dehydrogenase MPN017 (Mycoplasma pneumoniae strain M129 gene mtd1) 184657-58-7, Ribosomal S6 modification protein MPN016 (Mycoplasma pneumoniae strain M129 gene rimK) 184657-59-8, Protein MPN015 (Mycoplasma pneumoniae strain M129 gene D12-orf285) 184657-60-1, Protein MPN014 (Mycoplasma pneumoniae strain M129 gene dnaE) 184657-61-2, Protein MPN013 (Mycoplasma pneumoniae strain M129 gene D12-orf257) 184657-62-3, Protein MPN012 (Mycoplasma pneumoniae strain M129 gene D12-orf235) 184657-63-4, Protein MPN011 (Mycoplasma pneumoniae strain M129 gene D12-orf231) 184657-64-5, Protein MPN010 (Mycoplasma pneumoniae strain M129 gene D12-orf131) 184657-65-6, Hydrolase MPN009 Mycoplasma pneumoniae strain M129 gene yabD) 184657-66-7, Thiophene/furan oxidation protein MPN008 (Mycoplasma pneumoniae strain M129 gene thdF) 184657-67-8, DNA-polymerase (MPN007) (Mycoplasma pneumoniae strain M129 gene holB) 184657-68-9, Thymidylate kinase (MPN006) (Mycoplasma pneumoniae strain M129 gene D12-orf210) 184657-70-3, Seryl-tRNA synthetase (MPN005) (Mycoplasma pneumoniae strain M129 gene serS) 184657-71-4, DNA gyrase (MPN004) (Mycoplasma pneumoniae strain M129 gene gyrA subunit A) 184657-73-6, Protein MPN684 (Mycoplasma pneumoniae strain M129 gene K05-orf1882) 184657-74-7, ABC transporter MPN683 (Mycoplasma pneumoniae strain M129 gene devA subunit) 184657-75-8, RNase P MPN681 (Mycoplasma pneumoniae strain M129 gene rnpA C5 chain) 184657-76-9, Protein MPN680 (Mycoplasma pneumoniae strain M129 gene K05-orf385) 184657-82-7, S-Adenosylmethionine-6-N',N'-adenosyl(rRNA) dimethyltransferase MPN679 (Mycoplasma pneumoniae strain M129 gene ksgA) 184657-83-8, ATPase-like protein MPN677 (Mycoplasma pneumoniae strain M129 gene K05-orf425) 184657-84-9, Glutamyl-tRNA synthetase MPN678

(Mycoplasma pneumoniae strain M129 gene gltX) 184657-85-0, Protein MPN676 (Mycoplasma pneumoniae strain M129 gene K05-orf106) 184657-86-1, Protein MPN675 (Mycoplasma pneumoniae strain M129 gene K05-orf101a) 184657-87-2, L-Lactate dehydrogenase MPN674 (Mycoplasma pneumoniae strain M129 gene ldh) 184657-88-3, Protein MPN673 (Mycoplasma pneumoniae strain M129 gene K05-orf169) 184657-89-4, Hypoxanthine-guanine phosphoribosyltransferase MPN672 Mycoplasma pneumoniae strain M129 gene hpt) 184657-90-7, Cell division protein FtsH MPN671 (Mycoplasma pneumoniae strain M129 gene ftsH) 184657-91-8, Protein MPN670 (Mycoplasma pneumoniae strain M129 gene K05-orf345) 184657-92-9, Tyrosyl tRNA synthetase MPN669 (Mycoplasma pneumoniae strain M129 gene tyrS) 184657-93-0, Protein MPN668 (Mycoplasma pneumoniae strain M129 gene osmC) 184657-94-1, UDP-glucose pyrophosphorylase MPN667 (Mycoplasma pneumoniae strain M129 gene gtaB) 184657-95-2, Protein MPN666 (Mycoplasma pneumoniae strain M129 gene K05-orf251) 184657-97-4, Elongation factor Tu (MPN665) (Mycoplasma pneumoniae strain M129 gene tuf) 184657-98-5 184657-99-6, Protein MPN663 (Mycoplasma pneumoniae strain M129 gene K05-orf234) 184658-00-2, Protein MPN662 (Mycoplasma pneumoniae strain M129 gene pilB) 184658-02-4, Ribosomal protein S16 (MPN660) (Mycoplasma pneumoniae strain M129 gene rpsP) 184658-03-5, TRNA (guanine-N1)-methyltransferase MPN659 (Mycoplasma pneumoniae strain M129 gene trmD) 184658-04-6, Ribosomal protein L19 (MPN658) (Mycoplasma pneumoniae strain M129 gene rplS) 184658-05-7, Protein MPN657 (Mycoplasma pneumoniae strain M129 gene K05-orf401) 184658-06-8, GTP-binding protein-like protein MPN656 (Mycoplasma pneumoniae strain M129 gene K05-orf271) 184658-07-9, Protein MPN655 (Mycoplasma pneumoniae strain M129 gene E09-orf204o) 184658-08-0, Protein MPN654 (Mycoplasma pneumoniae strain M129 gene E09-orf129) 184691-95-0, Protein MPN653 (Mycoplasma pneumoniae strain M129 gene mtlF) 184691-96-1, Mannitol-1-phosphate 5-dehyrogenase MPN637 (Mycoplasma pneumoniae strain M129 gene mtlD) 184691-97-2, Protein MPN651 (Mycoplasma pneumoniae strain M129 gene mtlA) 184691-98-3, Protein MPN650 (Mycoplasma pneumoniae strain M129 gene E09-orf101) 184691-99-4, Protein MPN649 (Mycoplasma pneumoniae strain M129 gene E09-orf136L) 184692-00-0, Protein MPN648 (Mycoplasma pneumoniae strain M129 gene E09-orf136) 184692-01-1, Protein MPN647 (Mycoplasma pneumoniae strain M129 gene E09-orf290) 184692-02-2, Protein MPN646 (Mycoplasma pneumoniae strain M129 gene E09-orf277) 184692-03-3, Protein MPN645 (Mycoplasma pneumoniae strain M129 gene E09-orf283a) 184692-04-4, Protein MPN644 (Mycoplasma pneumoniae strain M129 gene E09-orf283b) 184692-05-5, Protein MPN643 (Mycoplasma pneumoniae strain M129 gene E09-orf302) 184692-06-6, Protein MPN642 (Mycoplasma pneumoniae strain M129 gene E09-orf279) 184692-07-7, Protein MPN641 (Mycoplasma pneumoniae strain M129 gene E09-orf276) 184692-08-8, Protein MPN640 (Mycoplasma pneumoniae strain M129 gene E09-orf300) 184692-09-9, Protein MPN639 (Mycoplasma pneumoniae strain M129 gene E09-orf287o) 184692-10-2, **Nuclease**, restriction endodeoxyribo-MPN638 (Mycoplasma pneumoniae strain M129 gene E30-orf375 specificity-**determining** subunit) 184692-11-3, CDP-diglyceride synthetase MPN637 (Mycoplasma pneumoniae strain M129 gene cdsA) 184692-12-4, Ribosome-releasing factor MPN636 (Mycoplasma pneumoniae strain M129 gene frr) 184692-13-5, Protein MPN635 (Mycoplasma pneumoniae strain M129 gene E30-orf352) 184692-14-6, Protein MPN634 (Mycoplasma pneumoniae strain M129 gene C12-orf181o) 184692-15-7, Protein MPN633 (Mycoplasma pneumoniae strain M129 gene C12-orf247) 184692-16-8, Uridylate kinase MPN632 (Mycoplasma pneumoniae strain M129 gene pyrH) 184692-17-9, Elongation factor Ts MPN631 (Mycoplasma pneumoniae strain M129 gene tsf) 184692-18-0, Protein MPN630 (Mycoplasma pneumoniae strain M129 gene yfiB) 184692-19-1, Triosephosphate isomerase MPN629 (Mycoplasma pneumoniae strain M129 gene tim) 184692-20-4, Protein MPN628 (Mycoplasma pneumoniae strain M129 gene pgm) 184692-21-5, PEP-dependent HPr protein kinase phosphoryltransferase (Enzyme I) MPN627

(Mycoplasma pneumoniae strain M129 gene ptsI) 184692-22-6, Protein MPN626 (Mycoplasma pneumoniae strain M129 gene C12-orf172) 184692-24-8, Protein MPN615 (Mycoplasma pneumoniae strain M129 gene hsdS) 184692-25-9, Protein MPN625 (Mycoplasma pneumoniae strain M129 gene C12-orf141) 184692-26-0, RNA helicase deaD-like protein MPN623 (Mycoplasma pneumoniae strain M129 gene deaD) 184692-27-1, Protein MPN622 (Mycoplasma pneumoniae strain M129 gene rpsO) 184692-28-2, Metallohydrolase-like protein MPN621 (Mycoplasma pneumoniae strain M129 gene C12-orf561) 184692-29-3, Protein MPN620 (Mycoplasma pneumoniae strain M129 gene C12-orf839) 184692-30-6, Excinuclease ABC (MPN619) (Mycoplasma pneumoniae strain M129 gene uvrA subunit A) 184692-31-7, .gamma.-Like MPN618 (Mycoplasma pneumoniae strain M129 gene dnaX) 184692-32-8, Ribosomal protein L13 MPN617 (Mycoplasma pneumoniae strain M129 gene rplM) 184692-33-9, Ribosomal protein S9 MPN616 (Mycoplasma pneumoniae strain M129 gene rpsI) 184692-34-0, Protein MPN614 (Mycoplasma pneumoniae strain M129 gene C12-orf334) 184692-35-1, Protein MPN613 (Mycoplasma pneumoniae strain M129 gene C12-orf344) 184692-36-2, Protein MPN612 (Mycoplasma pneumoniae strain M129 gene C12-orf997) 184692-37-3, Phosphate-binding protein PstS-like protein MPN611 (Mycoplasma pneumoniae strain M129 gene C12-orf385) 184692-38-4, Phosphate transporter MPN610 (Mycoplasma pneumoniae strain M129 gene pstA) 184692-39-5, Phosphate transporter MPN609 (Mycoplasma pneumoniae strain M129 gene pstB) 184692-40-8, Phosphate transport system regulatory protein MPN608 (Mycoplasma pneumoniae strain M129 gene phoU) 184692-41-9, Peptide methionine sulfoxide reductase MPN607 (Mycoplasma pneumoniae strain M129 gene pmsR) 184692-42-0, Enolase MPN606 (Mycoplasma pneumoniae strain M129 gene eno) 184692-43-1, Protein MPN594 (Mycoplasma pneumoniae strain M129 gene D02-orf122a) 184692-47-5 184692-50-0, Protein MPN586 (Mycoplasma pneumoniae strain M129 gene D02-orf347) 184692-51-1, Protein MPN585 (Mycoplasma pneumoniae strain M129 gene D02-orf302) 184692-52-2, Protein MPN584 (Mycoplasma pneumoniae strain M129 gene D02-orf135L) 184692-53-3, Protein MPN583 (Mycoplasma pneumoniae strain M129 gene D02-orf225L) 184692-54-4, Protein MPN582 (Mycoplasma pneumoniae strain M129 gene D02-orf439) 184692-55-5, Protein MPN581 (Mycoplasma pneumoniae strain M129 gene D02-orf265V) 184692-57-7, Protein MPN580 (Mycoplasma pneumoniae strain M129 gene D02-orf140) 184692-58-8, Protein MPN579 (Mycoplasma pneumoniae strain M129 gene D02-orf109) 184692-59-9, Protein MPN578 (Mycoplasma pneumoniae strain M129 gene D02-orf100) 184692-60-2, Serine hydroxymethyltransferase MPN576 (Mycoplasma pneumoniae strain M129 gene glyA) 184692-61-3, Protein MPN575 (Mycoplasma pneumoniae strain M129 gene D02-orf128) 184692-62-4, Heat shock protein MPN574 (Mycoplasma pneumoniae strain M129 gene groES) 184692-63-5, Heat shock protein GroEL MPN573 (Mycoplasma pneumoniae strain M129 gene groEL) 184692-64-6, Protein MPN572 (Mycoplasma pneumoniae strain M129 gene D02-orf445) 184692-65-7, Hemolysin ABC-type exporter MPN571 (Mycoplasma pneumoniae strain M129 gene lcnDR3) 184692-66-8, Protein MPN570 (Mycoplasma pneumoniae strain M129 gene D02-orf129) 184692-67-9, Hemolysin-interacting metalloenzyme MPN569 (Mycoplasma pneumoniae strain M129 gene D02-orf108) 184692-68-0, G Protein MPN568 (Mycoplasma pneumoniae strain M129 gene spg) 184692-69-1, Protein MPN567 (Mycoplasma pneumoniae strain M129 gene P200) 184692-70-4, Glycerophosphoryl diester phosphodiesterase MPN566 (Mycoplasma pneumoniae strain M129 gene glpQ) 184692-71-5, Protein MPN565 (Mycoplasma pneumoniae strain M129 gene H03-orf152) 184692-72-6, NADP-dependent alcohol dehydrogenase-like protein MPN564 (Mycoplasma pneumoniae strain M129 gene adh) 184692-73-7, Small GTPase MPN563 (Mycoplasma pneumoniae strain M129 gene obg) 184692-75-9, NH3-dependent **NAD** synthetase MPN562 (Mycoplasma pneumoniae strain M129 gene outB) 184692-76-0, **Uridine** kinase MPN561 (Mycoplasma pneumoniae strain M129 gene udk) 184692-77-1, Arginine deiminase MPN560

(Mycoplasma pneumoniae strain M129 gene arcA) 184692-86-2, Protein MPN559 (Mycoplasma pneumoniae strain M129 gene H03-orf235) 184692-87-3, Methyltransferase MPN558 (Mycoplasma pneumoniae strain M129 gene gidB) 184692-88-4, Dehydrogenase, reduced **nicotinamide** adenine dinucleotide (Mycoplasma pneumoniae strain M129 gene gidA) 184692-89-5, Arginyl-tRNA synthetase MPN556 (Mycoplasma pneumoniae strain M129 gene argS) 184692-90-8, Protein MPN555 (Mycoplasma pneumoniae strain M129 gene H03-orf193o) 184692-91-9, Protein MPN554 (Mycoplasma pneumoniae strain M129 gene G12-orf104) 184692-92-0, Threonyl-tRNA synthetase MPN553 (Mycoplasma pneumoniae strain M129 gene thrSv) 184692-93-1, Protein MPN552 (Mycoplasma pneumoniae strain M129 gene G12-orf269) 184692-94-2, Protein MPN551 (Mycoplasma pneumoniae strain M129 gene G12-orf281) 184692-95-3, Thiamin biosynthesis protein MPN550 (Mycoplasma pneumoniae strain M129 gene G12-orf387) 184692-96-4, Phosphodiesterase MPN549 (Mycoplasma pneumoniae strain M129 gene G12-orf325) 184692-97-5, Synthetase, ribosomal ribonucleate pseudouridine (Mycoplasma pneumoniae strain M129 gene G12-orf326) 184692-99-7, Kinase (phosphorylating), dihydroxyacetone (Mycoplasma pneumoniae strain M129 gene G12-orf558) 184693-01-4, Fatty acid/phospholipid synthesis protein PlsX MPN546 (Mycoplasma pneumoniae strain M129 gene plsX) 184693-02-5, Ribonuclease III MPN545 (Mycoplasma pneumoniae strain M129 gene rnc) 184693-03-6, Methionyl-tRNA formyltransferase MPN543 (Mycoplasma pneumoniae strain M129 gene fmt) 184693-04-7, Protein MPN542 (Mycoplasma pneumoniae strain M129 gene G12-orf218) 184693-05-8, Protein MPN544 (Mycoplasma pneumoniae strain M129 gene G12-orf664) 184693-12-7, Ribosomal protein S20 (MPN541) (Mycoplasma pneumoniae strain M129 gene rpsT) 184693-13-8, Ribosomal protein L7/L12 (MPN539) (Mycoplasma pneumoniae strain M129 gene rplL isoform A) 184693-14-9, Ribosomal protein L10 (MPN538) (Mycoplasma pneumoniae strain M129 gene rplJ) 184693-15-0, UV protection protein MucB (MPN537) (Mycoplasma pneumoniae strain M129 gene mucB) 184693-16-1, Holliday junction DNA helicase (MPN536) (Mycoplasma pneumoniae strain M129 gene ruvB) 184693-17-2, Holliday junction DNA helicase (MPN535) (Mycoplasma pneumoniae strain M129 gene ruvA) 184693-18-3, Protein MPN534 (Mycoplasma pneumoniae strain M129 gene G12-orf140b) 184693-19-4, Acetate kinase (MPN533) (Mycoplasma pneumoniae strain M129 gene ackA) 184693-20-7, Protein MPN532 (Mycoplasma pneumoniae strain M129 gene licA) 184693-21-8, ATP-dependent protease (MPN531) (Mycoplasma pneumoniae strain M129 gene clpB subunit) 184693-22-9, Protein MPN530 (Mycoplasma pneumoniae strain M129 gene G12-orf136) 184693-23-0, Histone-like protein MPN529 (Mycoplasma pneumoniae strain M129 gene G12-orf109) 184693-24-1, Inorganic pyrophosphatase MPN528 (Mycoplasma pneumoniae strain M129 gene ppa) 184693-25-2, Oxidoreductase (MPN527) (Mycoplasma pneumoniae strain M129 gene G12-orf225 membrane-integrated isoenzyme) 184693-26-3, Protein MPN526 (Mycoplasma pneumoniae strain M129 gene G12-orf328b) 184693-27-4, Protein MPN525 (Mycoplasma pneumoniae strain M129 gene G12-orf413) 184693-28-5, Protein MPN524 (Mycoplasma pneumoniae strain M129 gene G12-orf168) 184693-29-6, STARP antigen-like membrane protein MPN523 (Mycoplasma pneumoniae strain M129 gene G12-orf305) 184693-30-9, Methyltransferase-like protein MPN522 (Mycoplasma pneumoniae strain M129 gene G12-orf210V) 184693-33-2, Methyltransferase, ribosomal ribonucleate (MPN521) (Mycoplasma pneumoniae strain M129 gene ygl3) 184693-35-4, Isoleucine-tRNA ligase MPN520 (Mycoplasma pneumoniae strain M129 gene ileS) 184693-37-6, Triacylglycerol lipase MPN519 (Mycoplasma pneumoniae strain M129 gene lip3) 184693-38-7, Protein MPN518 (Mycoplasma pneumoniae strain M129 gene G12-orf348) 184693-39-8, Reductase-like protein MPN517 (Mycoplasma pneumoniae strain M129 gene G12-orf166a) 184693-40-1, RNA polymerase MPN516 (Mycoplasma pneumoniae strain M129 gene rpoB subunit .beta.) 184693-41-2, DNA-dependent RNA polymerase MPN515 (Mycoplasma pneumoniae strain M129 gene rpoC .beta.'-chain) 184693-42-3, Protein MPN514 (Mycoplasma pneumoniae strain

M129 gene F04-orf120) 184693-43-4, Protein MPN513 (Mycoplasma pneumoniae strain M129 gene F04-orf150) 184693-44-5, Membrane export protein MPN512 (Mycoplasma pneumoniae strain M129 gene F04-orf154) 184693-45-6, Membrane export protein MPN511 (Mycoplasma pneumoniae strain M129 gene F04-orf260V) 184693-46-7, Membrane export protein MPN510 (Mycoplasma pneumoniae strain M129 gene P02-orf458) 184693-47-8, Membrane export protein MPN509 (Mycoplasma pneumoniae strain M129 gene P02-orf427) 184693-48-9, Membrane export protein MPN508 (Mycoplasma pneumoniae strain M129 gene P02-orf509) 184693-51-4, EcoKI restriction endonuclease-like protein MPN507 (Mycoplasma pneumoniae strain M129 gene P02-orf363V) 184693-52-5, Protein MPN506 (Mycoplasma pneumoniae strain M129 gene P02-orf793) 184693-53-6, Protein MPN505 (Mycoplasma pneumoniae strain M129 gene P02-orf253) 184693-54-7, Protein MPN504 (Mycoplasma pneumoniae strain M129 gene P02-orf126) 184693-55-8, Cytadherence-associated protein MPN503 (Mycoplasma pneumoniae strain M129 gene P02-orf381) 184693-58-1, Protein MPN502 (Mycoplasma pneumoniae strain M129 gene P02-orf422V) 184693-59-2, Protein MPN501 (Mycoplasma pneumoniae strain M129 gene P02-orf196) 184693-60-5, Protein MPN500 (Mycoplasma pneumoniae strain M129 gene P02-orf527V) 184693-61-6, Protein MPN499 (Mycoplasma pneumoniae strain M129 gene P02-orf163) 184693-67-2, L-Ribulose-5-phosphate 4-epimerase MPN498 (Mycoplasma pneumoniae strain M129 gene araD) 184693-70-7, Phosphotriesterase-like protein MPN497 (Mycoplasma pneumoniae strain M129 gene P02-orf143) 184693-71-8, Pentitol phosphotransferase-like protein MPN496 (Mycoplasma pneumoniae strain M129 gene yjfS) 184693-72-9

, Similar to phosphotransferase protein II, component A, for pentitol, SGAT MPN494 (Mycoplasma pneumoniae strain M129 gene yjfU) 184693-73-0, 3-Hexulose-6-phosphate synthase MPN493 (Mycoplasma pneumoniae strain M129 gene yjfV) 184693-74-1, Similar to D-ARABINO-6-HEXULOSE 3-PHOSPHATE isomerase from E.coli MPN492 (Mycoplasma pneumoniae strain M129 gene yjfW) 184693-75-2, Membrane **nuclease** MPN491 (Mycoplasma pneumoniae strain M129 gene P02-orf474) 184693-76-3, Protein MPN490 (Mycoplasma pneumoniae strain M129 gene recA) 184693-77-4, Lipoprotein MPN489 (Mycoplasma pneumoniae strain M129 gene P02-orf1300) 184693-80-9, N-Utilization substance protein A (MPN154) (Mycoplasma pneumoniae strain M129 gene nusA) 184693-81-0, Protein MPN163 (Mycoplasma pneumoniae strain M129 gene VXpSPT7-orf112) 184693-82-1, Protein MPN162 (Mycoplasma pneumoniae strain M129 gene VXpSPT7-orf320) 184693-83-2, Protein MPN161 (Mycoplasma pneumoniae strain M129 gene VXpSPT7-orf445) 184693-84-3, Protein MPN160 (Mycoplasma pneumoniae strain M129 gene VXpSPT7-orf377) 184693-85-4, Protein MPN159 (Mycoplasma pneumoniae strain M129 gene hlyC) 184693-86-5, Adenylyltransferase, **riboflavin** mononucleotide (Mycoplasma pneumoniae strain M129 gene yaaC) 184693-87-6, Protein MPN157 (Mycoplasma pneumoniae strain M129 gene VXpSPT7-orf402)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(re-annotating Mycoplasma pneumoniae genome sequence: adding value, function and reading frames)

IT 184693-88-7, Ribosome-binding factor A (MPN156) (Mycoplasma pneumoniae strain M129 gene rbfA) 184693-89-8, Protein synthesis initiation factor 2 (MPN155) (Mycoplasma pneumoniae strain M129 gene infB) 184719-97-9 184721-11-7, Ribosomal protein L16 (MPN172) (Mycoplasma pneumoniae strain M129 gene rplP) 184721-12-8, Ribosomal protein S3 (MPN171) (Mycoplasma pneumoniae strain M129 gene rpsC) 184721-13-9, Ribosomal protein L22 (MPN170) (Mycoplasma pneumoniae strain M129 gene rplV) 184721-14-0, Ribosomal protein S19 (MPN169) (Mycoplasma pneumoniae strain M129 gene rpsS) 184721-15-1, Ribosomal protein L2 (MPN168) (Mycoplasma pneumoniae strain M129 gene rplB) 184721-16-2, Ribosomal protein L23 (MPN167) (Mycoplasma pneumoniae strain M129 gene rplW) 184721-17-3, Ribosomal protein L4 (MPN166) (Mycoplasma pneumoniae strain M129 gene rplD)

184721-18-4, Ribosomal protein L3 (MPN165) (Mycoplasma pneumoniae strain M129 gene rplC) 184721-19-5, Ribosomal protein S10 (MPN164) (Mycoplasma pneumoniae strain M129 gene rpsJ) 184721-20-8, PTS system protein MPN207 (Mycoplasma pneumoniae strain M129 gene ptsG glucose-specific subunit IIABC) 184721-21-9, Protein MPN206 (Mycoplasma pneumoniae strain M129 gene GT9-orf113) 184721-22-0, Protein MPN205 (Mycoplasma pneumoniae strain M129 gene GT9-orf438V) 184721-23-1, Protein MPN204 (Mycoplasma pneumoniae strain M129 gene GT9-orf148) 184721-25-3, Protein MPN214 (Mycoplasma pneumoniae strain M129 gene G07-orf138) 184721-26-4, Protein MPN213 (Mycoplasma pneumoniae strain M129 gene G07-orf1030) 184721-27-5, Protein MPN212 (Mycoplasma pneumoniae strain M129 gene G07-orf135) 184721-28-6, Excinuclease ABC MPN211 (Mycoplasma pneumoniae strain M129 gene uvrB subunit B) 184721-29-7, Preprotein translocase MPN210 (Mycoplasma pneumoniae strain M129 gene secA) 184721-32-2, Cation-transporting P-type ATPase (MPN209) (Mycoplasma pneumoniae strain M129 gene mgtA) 184721-33-3, Ribosomal protein S2 (MPN208) (Mycoplasma pneumoniae strain M129 gene rpsB) 184721-34-4, Protein MPN241 (Mycoplasma pneumoniae strain M129 gene K04-orf280) 184721-35-5, Thioredoxin reductase MPN240 (Mycoplasma pneumoniae strain M129 gene trxB) 184721-36-6, Protein MPN239 (Mycoplasma pneumoniae strain M129 gene K04-orf222) 184721-37-7, Amidotransferase, glutamyl-transfer ribonucleate (glutamine-specific) (Mycoplasma pneumoniae strain M129 gene gatB subunit B) 184721-38-8, Amidotransferase, glutamyl-transfer ribonucleate (glutamine-specific) (Mycoplasma pneumoniae strain M129 gene gatA subunit A) 184721-39-9, Amidotransferase, glutamyl-transfer ribonucleate (glutamine-specific) (Mycoplasma pneumoniae strain M129 gene G07-orf479 subunit C) 184721-40-2, Uracil DNA glycosylase MPN235 (Mycoplasma pneumoniae strain M129 gene ung) 184721-41-3, Membrane export protein MPN234 (Mycoplasma pneumoniae strain M129 gene G07-orf417) 184721-45-7, Excreted protein MPN233 (Mycoplasma pneumoniae strain M129 gene G07-orf454) 184721-47-9, Ribosomal protein L9 (MPN231) (Mycoplasma pneumoniae strain M129 gene rplI) 184721-52-6, Ribosomal protein S18 (MPN230) (Mycoplasma pneumoniae strain M129 gene rpsR) 184721-53-7, Ribosomal protein S6 (MPN228) (Mycoplasma pneumoniae strain M129 gene rpsF) 184721-54-8, Ribosomal protein S7 (MPN226) (Mycoplasma pneumoniae strain M129 gene rpsG) 184721-55-9, SsDNA-binding protein MPN229 (Mycoplasma pneumoniae strain M129 gene ssb) 184721-57-1, Replicative DNA helicase MPN232 (Mycoplasma pneumoniae strain M129 gene dnaB) 184721-59-3, Elongation factor G MPN227 (Mycoplasma pneumoniae strain M129 gene fus) 184721-60-6, Ribosomal protein S12 (MPN225) (Mycoplasma pneumoniae strain M129 gene rpsL) 184721-61-7, Prolipoprotein diacylglyceryl transferase MPN224 (Mycoplasma pneumoniae strain M129 gene lgt) 184721-62-8, Kinase (phosphorylating), phosphocarrier protein HPr (serine) (MPN223) (Mycoplasma pneumoniae strain M129 gene G07-orf312) 184721-63-9, Cell cycle protein-like protein MesJ MPN222 (Mycoplasma pneumoniae strain M129 gene yacA) 184721-64-0, Peptidyl-tRNA hydrolase MPN221 (Mycoplasma pneumoniae strain M129 gene pth) 184721-65-1, Ribosomal protein L11 (MPN219) (Mycoplasma pneumoniae strain M129 gene rplK) 184721-66-2, Oligopeptide transporter MPN218 (Mycoplasma pneumoniae strain M129 gene oppF) 184721-67-3, Ribosomal protein L1 (MPN220) (Mycoplasma pneumoniae strain M129 gene rplA) 184721-68-4, Oligopeptide transporter MPN217 (Mycoplasma pneumoniae strain M129 gene oppD) 184721-69-5, Oligopeptide transporter MPN216 (Mycoplasma pneumoniae strain M129 gene amiD) 184721-70-8, Oligopeptide transporter MPN215 (Mycoplasma pneumoniae strain M129 gene oppB) 184721-72-0, Phosphatidylglycerophosphate synthase MPN253 (Mycoplasma pneumoniae strain M129 gene pgsA) 184721-73-1, Asparaginyl-tRNA synthetase MPN252 (Mycoplasma pneumoniae strain M129 gene asnS) 184721-74-2, D-Ribulose-5-phosphate 3 epimerase MPN251 (Mycoplasma pneumoniae strain M129 gene cfxE) 184721-75-3, Protein MPN250 (Mycoplasma pneumoniae

strain M129 gene pgiB) 184721-76-4, GTP/ATP-binding protein-like protein MPN249 (Mycoplasma pneumoniae strain M129 gene yjeQ) 184721-77-5, Ser/Thr/Tyr protein kinase MPN248 (Mycoplasma pneumoniae strain M129 gene K04-orf389) 184721-78-6, Protein phosphatase 2C-like protein MPN247 (Mycoplasma pneumoniae strain M129 gene ptc1) 184721-79-7, Membrane-associated guanylate kinase MPN246 (Mycoplasma pneumoniae strain M129 gene gmk) 184721-80-0, Polypeptide deformylase MPN245 (Mycoplasma pneumoniae strain M129 gene def) 184721-81-1, Protein MPN244 (Mycoplasma pneumoniae strain M129 gene K04-orf202) 184721-82-2, **Nuclease**, exoribo- (Mycoplasma pneumoniae strain M129 gene vacB) 184721-84-4, Nucleotide-binding protein MPN269 (Mycoplasma pneumoniae strain M129 gene ysr1) 184721-85-5, PTS Pentitol phosphotransferase EIIB/EIIC-like protein MPN268 (Mycoplasma pneumoniae strain M129 gene A65-orf117) 184721-86-6, Protein MPN267 (Mycoplasma pneumoniae strain M129 gene A65-orf259) 184721-87-7, Oxido/arsenate reductase-like protein MPN266 (Mycoplasma pneumoniae strain M129 gene ygl1) 184721-88-8, Tryptophanyl-tRNA synthetase MPN265 (Mycoplasma pneumoniae strain M129 gene trpS) 184721-89-9, Phosphate hydrolyzing-like sequence-containing protein MPN264 (Mycoplasma pneumoniae strain M129 gene A65-orf281) 184721-90-2, Thioredoxin MPN263 (Mycoplasma pneumoniae strain M129 gene trx) 184721-91-3, Reticulocyte-binding protein-like protein MPN262 (Mycoplasma pneumoniae strain M129 gene A65-orf475) 184721-92-4, DNA topoisomerase I MPN261 (Mycoplasma pneumoniae strain M129 gene topA) 184721-93-5, Sugar (ribose/galactose) transporter (Mycoplasma pneumoniae strain M129 gene rbsC) 184721-94-6, Sugar (ribose/galactose) transporter (Mycoplasma pneumoniae strain M129 gene A65-orf517) 184721-96-8, Sugar (ribose/galactose) transporter MPN258 (Mycoplasma pneumoniae strain M129 gene yjcW subunit) 184721-97-9, UDP-glucose 4-epimerase MPN257 (Mycoplasma pneumoniae strain M129 gene galE) 184721-98-0, Protein MPN256 (Mycoplasma pneumoniae strain M129 gene A65-orf223) 184721-99-1, Protein MPN255 (Mycoplasma pneumoniae strain M129 gene A65-orf251b) 184722-00-7, GTP-binding membrane protein MPN279 (Mycoplasma pneumoniae strain M129 gene lepA) 184722-01-8, Mutase, **uridine** diphosphogalactopyranose (Mycoplasma pneumoniae strain M129 gene yefE) 184722-02-9, Lysyl-tRNA synthetase MPN277 (Mycoplasma pneumoniae strain M129 gene lysS) 184722-03-0, Protein MPN276 (Mycoplasma pneumoniae strain M129 gene A65-orf285) 184722-04-1, Protein MPN275 (Mycoplasma pneumoniae strain M129 gene yaaK) 184722-05-2, Molybdenum-sulfate transporter (Mycoplasma pneumoniae strain M129 gene A65-orf266 subunit) 184722-06-3, Nucleotidyl hydrolases/transferase MPN273 (Mycoplasma pneumoniae strain M129 gene hit1) 184722-07-4, EcoK restriction endonuclease MPN285 (Mycoplasma pneumoniae strain M129 gene prrB) 184722-08-5, Protein MPN284 (Mycoplasma pneumoniae strain M129 gene A65-orf794) 184722-09-6, Protein MPN283 (Mycoplasma pneumoniae strain M129 gene A65-orf115) 184722-10-9, Protein MPN282 (Mycoplasma pneumoniae strain M129 gene A65-orf166) 184722-11-0, Protein MPN281 (Mycoplasma pneumoniae strain M129 gene A65-orf377) 184722-12-1, SsRNA/DNA-processing enzyme-like protein MPN280 (Mycoplasma pneumoniae strain M129 gene A65-orf569) 184722-14-3, Protein MPN295 (Mycoplasma pneumoniae strain M129 gene H10-orf220L) 184722-15-4, Protein MPN294 (Mycoplasma pneumoniae strain M129 gene H10-orf206) 184722-16-5, Prolipoprotein signal peptidase MPN293 (Mycoplasma pneumoniae strain M129 gene lsp) 184722-17-6, Large subunit pseudouridine synthase D-like protein MPN292 (Mycoplasma pneumoniae strain M129 gene yceC) 184722-19-8, Protein MPN291 (Mycoplasma pneumoniae strain M129 gene H10-orf196) 184722-20-1, Protein MPN390 (Mycoplasma pneumoniae strain M129 gene H10-orf145L) 184722-21-2, EcoKI restriction endonuclease MPN289 (Mycoplasma pneumoniae strain M129 gene hsdS1B) 184722-22-3, Protein MPN288 (Mycoplasma pneumoniae strain M129 gene A65-orf787o) 184722-23-4, Protein MPN287 (Mycoplasma pneumoniae strain M129 gene

A65-orf118) 184722-24-5, Protein MPN286 (Mycoplasma pneumoniae strain M129 gene A65-orf465V) 184785-71-5, Ribosomal protein L32 (MPN540) (Mycoplasma pneumoniae strain M129 gene rpmF) 184785-73-7, Ribosomal protein L28 (MPN624) (Mycoplasma pneumoniae strain M129 gene rpmB) 184786-52-5, Amino acid tranporter MPN308 (Mycoplasma pneumoniae strain M129 gene F10-orf565) 184786-53-6, Carbamate kinase MPN307 (Mycoplasma pneumoniae strain M129 gene arcC) 184786-54-7, Protein MPN306 (Mycoplasma pneumoniae strain M129 gene argI) 184786-55-8, Protein MPN305 (Mycoplasma pneumoniae strain M129 gene arcA) 184786-56-9, Protein MPN304 (Mycoplasma pneumoniae strain M129 gene arcA) 184786-59-2, Pyruvate kinase MPN303 (Mycoplasma pneumoniae strain M129 gene pyk) 184786-60-5, 6-Phosphofructokinase MPN302 (Mycoplasma pneumoniae strain M129 gene pfk) 184786-61-6, Protein MPN301 (Mycoplasma pneumoniae strain M129 gene ypuH) 184786-62-7, Protein MPN300 (Mycoplasma pneumoniae strain M129 gene dyr) 184786-63-8, 1-Acyl-sn-glycerol-3-phosphate acyltransferase MPN299 (Mycoplasma pneumoniae strain M129 gene plsB) 184786-64-9, Protein MPN297 (Mycoplasma pneumoniae strain M129 gene H10-orf149) 184786-65-0, Holo-[acyl carrier protein] synthase-like protein MPN298 (Mycoplasma pneumoniae strain M129 gene H10-orf119) 184786-66-1, Amino acid transporter-like protein MPN319 (Mycoplasma pneumoniae strain M129 gene gap1) 184786-67-2, Amino acid transporter MPN318 (Mycoplasma pneumoniae strain M129 gene F10-orf491) 184786-68-3, Cell division protein MPN317 (Mycoplasma pneumoniae strain M129 gene ftsZ) 184786-69-4, Protein MPN316 (Mycoplasma pneumoniae strain M129 gene F10-orf419) 184786-70-7, S-Adenosylmethionine-dependent methytransferase MPN315 (Mycoplasma pneumoniae strain M129 gene yabC) 184786-71-8, Protein MPN314 (Mycoplasma pneumoniae strain M129 gene yabB) 184786-72-9, Protein MPN313 (Mycoplasma pneumoniae strain M129 gene F10-orf90) 184786-73-0, Protein MPN312 (Mycoplasma pneumoniae strain M129 gene F10-orf218) 184786-74-1, Protein MPN311 (Mycoplasma pneumoniae strain M129 gene F10-orf357) 184786-75-2, Cytadherence high-molecular-weight protein 2 (MPN310) (Mycoplasma pneumoniae strain M129 gene F10-orf1818) 184786-76-3, ATP-dependent Lon protease (MPN332) (Mycoplasma pneumoniae strain M129 gene lon) 184786-77-4, Trigger factor MPN331 (Mycoplasma pneumoniae strain M129 gene tig) 184786-78-5, Protein MPN330 (Mycoplasma pneumoniae strain M129 gene F10-orf294) 184786-79-6, Ferric uptake regulator MPN329 (Mycoplasma pneumoniae strain M129 gene F10-orf158) 184786-80-9, Endonuclease IV MPN328 (Mycoplasma pneumoniae strain M129 gene nfo) 184786-81-0, Ribosomal protein L27 (MPN327) (Mycoplasma pneumoniae strain M129 gene rpmA) 184786-82-1, Protein MPN326 (Mycoplasma pneumoniae strain M129 gene ysxB) 184786-83-2, Ribosomal protein L21 (MPN325) (Mycoplasma pneumoniae strain M129 gene rplU) 184786-84-3, Ribonucleoside-diphosphate reductase MPN324 (Mycoplasma pneumoniae strain M129 gene nrdE .alpha.-chain) 184786-85-4, NrdI-like protein MPN323 (Mycoplasma pneumoniae strain M129 gene F10-orf153) 184786-86-5, Ribonucleoside diphosphate reductase MPN322 (Mycoplasma pneumoniae strain M129 gene nrdF .beta.-chain) 184786-87-6, Dihydrofolate reductase MPN321 (Mycoplasma pneumoniae strain M129 gene dhfr) 184786-88-7, Thymidylate synthase MPN320 (Mycoplasma pneumoniae strain M129 gene thyA) 184786-89-8, DNA helicase II MPN340 (Mycoplasma pneumoniae strain M129 gene pcrA) 184786-90-1, Protein MPN339 (Mycoplasma pneumoniae strain M129 gene H91-orf224) 184786-91-2, Protein MPN338 (Mycoplasma pneumoniae strain M129 gene F10-orf632o) 184786-92-3, Protein MPN337 (Mycoplasma pneumoniae strain M129 gene F10-orf621) 184786-94-5, Protein MPN335 (Mycoplasma pneumoniae strain M129 gene F10-orf741) 184786-95-6, ABC (ATP-binding cassette-containing) transporter MPN334 (Mycoplasma pneumoniae strain M129 gene bcrA) 184786-96-7, Protein MPN333 (Mycoplasma pneumoniae strain M129 gene F10-orf750) 184786-97-8, Type I restriction enzyme MPN347 (Mycoplasma

pneumoniae strain M129 gene hsdR) 184786-98-9, Type I restriction enzyme hsdR MPN346 (Mycoplasma pneumoniae strain M129 gene H91-orf115) 184786-99-0, Type I restriction enzyme MPN345 (Mycoplasma pneumoniae strain M129 gene hsdR) 184787-00-6, Protein MPN344 (Mycoplasma pneumoniae strain M129 gene H91-orf216) 184787-01-7, Protein MPN343 (Mycoplasma pneumoniae strain M129 gene H91-orf330) 184787-02-8, Type I restriction enzyme HsdM MPN342 (Mycoplasma pneumoniae strain M129 gene hsdM) 184787-03-9, DNA helicase II MPN341 (Mycoplasma pneumoniae strain M129 gene mutB1) 184787-04-0, Protein MPN364 (Mycoplasma pneumoniae strain M129 gene H91-orf677) 184787-05-1, Protein MPN363 (Mycoplasma pneumoniae strain M129 gene H91-orf102) 184787-06-2, HemK family enzyme MPN362 (Mycoplasma pneumoniae strain M129 gene H91-orf453) 184787-09-5, Peptide chain release factor 1 (MPN361) (Mycoplasma pneumoniae strain M129 gene prfA) 184787-10-8, Ribosomal protein L31 (MPN360) (Mycoplasma pneumoniae strain M129 gene rpmE) 184787-11-9, Protein MPN359 (Mycoplasma pneumoniae strain M129 gene H91-orf258) 184787-12-0, Protein MPN358 (Mycoplasma pneumoniae strain M129 gene H91-orf534) 184787-13-1, DNA ligase MPN357 (Mycoplasma pneumoniae strain M129 gene lig) 184787-14-2, Cysteinyl-tRNA synthetase MPN356 (Mycoplasma pneumoniae strain M129 gene cysS) 184787-15-3, Protein MPN355 (Mycoplasma pneumoniae strain M129 gene yacO) 184787-16-4, Glycyl-tRNA synthetase MPN354 (Mycoplasma pneumoniae strain M129 gene grs1) 184787-17-5, DNA primase MPN353 (Mycoplasma pneumoniae strain M129 gene dnaE) 184787-18-6, .sigma.-70 Transcription factor family protein MPN352 (Mycoplasma pneumoniae strain M129 gene sigA) 184787-19-7, Methyltransferase MPN351 (Mycoplasma pneumoniae strain M129 gene H91-orf213) 184787-20-0, Protein MPN350 (Mycoplasma pneumoniae strain M129 gene ygiH) 184787-21-1, Protein MPN349 (Mycoplasma pneumoniae strain M129 gene H91-orf281) 184787-22-2, 5-Formyltetrahydrofolate cycloligase MPN348 (Mycoplasma pneumoniae strain M129 gene H91-orf164) 184787-24-4, Protein MPN373 (Mycoplasma pneumoniae strain M129 gene A19-orf204) 184787-25-5, Pertussis toxin subunit s1-like protein MPN372 (Mycoplasma pneumoniae strain M129 gene A19-orf591) 184787-26-6, Protein MPN371 (Mycoplasma pneumoniae strain M129 gene A19-orf211) 184787-27-7, Protein MPN370 (Mycoplasma pneumoniae strain M129 gene A19-orf737V) 184787-28-8, Protein MPN369 (Mycoplasma pneumoniae strain M129 gene H91-orf253) 184787-29-9, Protein MPN368 (Mycoplasma pneumoniae strain M129 gene H91-orf180) 184787-30-2, Cytadherence-associated protein MPN367 (Mycoplasma pneumoniae strain M129 gene H91-orf322) 184787-32-4, Cytadherence-associated protein MPN366 (Mycoplasma pneumoniae strain M129 gene H91-orf272) 184787-33-5, Protein MPN365 (Mycoplasma pneumoniae strain M129 gene H91-orf268) 184787-34-6, Formamidopyrimidine-DNA glycosylase MPN380 (Mycoplasma pneumoniae strain M129 gene fpg) 184787-35-7, 5'-3' Exonuclease MPN379 (Mycoplasma pneumoniae strain M129 gene polA) 184787-36-8, DNA polymerase III MPN378 (Mycoplasma pneumoniae strain M129 gene dnaE subunit .alpha.) 184787-37-9, Protein MPN376 (Mycoplasma pneumoniae strain M129 gene A19-orf1140) 184787-38-0, Protein MPN375 (Mycoplasma pneumoniae strain M129 gene A19-orf129) 184787-39-1, Protein MPN374 (Mycoplasma pneumoniae strain M129 gene A19-orf229V) 184787-41-5, **NADH** oxidase MPN394 (Mycoplasma pneumoniae strain M129 gene nox) 184787-42-6, Pyruvate dehydrogenase MPN393 (Mycoplasma pneumoniae strain M129 gene pdhA subunit E1-.alpha.) 184787-45-9, Pyruvate dehydrogenase MPN392 (Mycoplasma pneumoniae strain M129 gene pdhB subunit E1-.beta.) 184787-46-0, Dihydrolipoamide acetyltransferase MPN391 (Mycoplasma pneumoniae strain M129 gene pdhC) 184787-47-1, Dihydrolipoamide dehydrogenase MPN390 (Mycoplasma pneumoniae strain M129 gene pdhD) 184787-48-2, Lipoate protein ligase MPN389 (Mycoplasma pneumoniae strain M129 gene lplA) 184787-49-3, Protein MPN387 (Mycoplasma pneumoniae strain M129 gene F11-orf358b) 184787-50-6, Kinase (phosphorylating), deoxyadenosine (MPN386) (Mycoplasma pneumoniae

strain M129 gene yaaF) 184787-51-7, Protein MPN385 (Mycoplasma pneumoniae strain M129 gene F11-orf114) 184787-52-8, Leucyl-tRNA synthetase MPN384 (Mycoplasma pneumoniae strain M129 gene leuS) 184787-53-9, HAD superfamily hydrolase/phosphatase MPN383 (Mycoplasma pneumoniae strain M129 gene yidA) 184787-54-0, Protein MPN382 (Mycoplasma pneumoniae strain M129 gene A19-orf200) 184787-55-1, HAD superfamily hydrolase/phosphatase MPN381 (Mycoplasma pneumoniae strain M129 gene yidA)

184787-56-2, Prolyl-tRNA synthetase MPN402 (Mycoplasma pneumoniae strain M129 gene proS) 184787-58-4, Transcription elongation factor GreA (MPN401) (Mycoplasma pneumoniae strain M129 gene greA) 184787-59-5, Protein MPN400 (Mycoplasma pneumoniae strain M129 gene F11-orf582) 184787-60-8, Protein MPN399 (Mycoplasma pneumoniae strain M129 gene F11-orf287) 184787-61-9, Protein MPN398 (Mycoplasma pneumoniae strain M129 gene F11-orf218) 184787-62-0, Pyrophosphatase, **guanosine** 3',5'-bis(diphosphate) 3'- (MPN397) (Mycoplasma pneumoniae strain M129 gene spoT) 184787-64-2, Protein MPN411 (Mycoplasma pneumoniae strain M129 gene A05-orf252) 184787-65-3, Protein MPN410 (Mycoplasma pneumoniae strain M129 gene F11-orf148o) 184787-66-4, Protein MPN409 (Mycoplasma pneumoniae strain M129 gene F11-orf533L) 184787-67-5, Protein MPN408 (Mycoplasma pneumoniae strain M129 gene F11-orf760) 184787-68-6, Lipase MPN407 (Mycoplasma pneumoniae strain M129 gene F11-orf879) 184787-69-7, Acyl-carrier protein MPN406 (Mycoplasma pneumoniae strain M129 gene F11-orf84) 184787-70-0, Protein MPN405 (Mycoplasma pneumoniae strain M129 gene F11-orf197) 184787-71-1, Protein MPN404 (Mycoplasma pneumoniae strain M129 gene F11-orf346) 184787-83-5, Protein MPN403 (Mycoplasma pneumoniae strain M129 gene F11-orf122a) 184787-84-6, Transporter MPN421 (Mycoplasma pneumoniae strain M129 gene A05-orf475) 184787-85-7, Glycerophosphoryl diester phosphodiesterase MPN420 (Mycoplasma pneumoniae strain M129 gene glpQ) 184787-86-8, Alanyl-tRNA synthetase MPN419 (Mycoplasma pneumoniae strain M129 gene alaS) 184787-87-9, Transporter MPN417 (Mycoplasma pneumoniae strain M129 gene P69) 184787-88-0, ATP-binding protein MPN416 (Mycoplasma pneumoniae strain M129 gene P29) 184787-89-1, High-affinity transport system protein MPN415 (Mycoplasma pneumoniae strain M129 gene P37) 184787-90-4, Cytadherence-associated protein MPN414 (Mycoplasma pneumoniae strain M129 gene A05-orf493) 184787-91-5, ABC (ATP-binding cassette-containing) transporter MPN433 (Mycoplasma pneumoniae strain M129 gene cbiO) 184787-92-6, ABC (ATP-binding cassette-containing) transporter MPN432 (Mycoplasma pneumoniae strain M129 gene artP) 184787-93-7, Transporter MPN431 (Mycoplasma pneumoniae strain M129 gene A05-orf317) 184787-94-8, Glycerladehyde-3-phosphate dehydrogenase MPN430 (Mycoplasma pneumoniae strain M129 gene gap) 184787-95-9, Phosphoglycerate kinase MPN429 (Mycoplasma pneumoniae strain M129 gene pgk) 184787-96-0, Phosphotransacetylase MPN428 (Mycoplasma pneumoniae strain M129 gene pta) 184787-97-1, Hydrolase/phosphatase MPN427 (Mycoplasma pneumoniae strain M129 gene yidA) 184787-98-2, SMC family protein MPN426 (Mycoplasma pneumoniae strain M129 gene A05-orf982) 184787-99-3, Cell division protein MPN425 (Mycoplasma pneumoniae strain M129 gene ftsY) 184788-00-9, Protein MPN424 (Mycoplasma pneumoniae strain M129 gene ylxM) 184788-01-0, Protein MPN423 (Mycoplasma pneumoniae strain M129 gene A05-orf129) 184788-02-1, TRNA 5-methylaminomethyl-2-thiouridylate methyltransferase MPN422 (Mycoplasma pneumoniae strain M129 gene A05-orf370) 184788-03-2, Protein MPN441 (Mycoplasma pneumoniae strain M129 gene H08-orf102) 184788-05-4, Chaperonin DnaK (MPN434) (Mycoplasma pneumoniae strain M129 gene dnaK) 184788-06-5, Protein MPN440 (Mycoplasma pneumoniae strain M129 gene H08-orf726) 184788-07-6, Mollicute-specific lipoprotein MPN439 (Mycoplasma pneumoniae strain M129 gene H08-orf237) 184788-08-7, Mollicute-specific lipoprotein MPN438 (Mycoplasma pneumoniae strain M129 gene H08-orf345) 184788-09-8,

Mollicute-specific lipoprotein MPN437 (Mycoplasma pneumoniae strain M129 gene H08-orf572o) 184788-10-1, Transport protein MPN435 (Mycoplasma pneumoniae strain M129 gene A05-orf395) 184788-11-2 184788-12-3, Triacylglycerol lipase MPN445 (Mycoplasma pneumoniae strain M129 gene lip3)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(re-annotating Mycoplasma pneumoniae genome sequence: adding value, function and reading frames)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:592856 HCAPLUS
DOCUMENT NUMBER: 133:173995
TITLE: **Determination** of **nuclease activity** and use in **assays**
INVENTOR(S): Harbron, Stuart
PATENT ASSIGNEE(S): UK
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000049172	A1	20000824	WO 2000-GB606	20000221
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2347213	A1	20000830	GB 1999-3851	19990220
EP 1155143	A1	20011121	EP 2000-903907	20000221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: GB 1999-3851 A 19990220
WO 2000-GB606 W 20000221

AB A method for detecting a nuclease enzyme is disclosed comprising the steps: (a) contacting said enzyme with a compd. of formula RpX, wherein R is a 3' nucleosidyl deriv., p is a phospho radical, and X is an esterifiable moiety or, only if R is a 3' nicotinamide deriv., X is an esterifiable moiety or H, whereby ROH and pX are produced, and (b) detecting said pX moiety or, only if R is a 3' nicotinamide deriv., detecting the pX moiety or the ROH moiety. In preferred embodiments the invention provides a method for detecting a nuclease enzyme that is free in soln., immobilized on a surface, or attached to a member of a specific binding pair. The method of the invention may thus be applied as a detection step in nucleic acid hybridization assays, enzyme immunoassays and ligand:receptor binding assays. The invention provides a variety of methods for detecting the detectable moieties produced. These include fluorometric, colorimetric, and luminometric endpoints. Enzyme cycling and apoenzyme reactivation assays are also provided.

IC ICM C12Q001-34

CC 7-1 (Enzymes)
Section cross-reference(s): 9
ST **nuclease detn**; biochem **assay**
nuclease detn; **apoenzyme** reactivation
assay; enzyme cycling **assay**
IT Enzymes, biological studies
RL: ARG (Analytical reagent use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **ANST (Analytical study)**; BIOL (Biological study); USES (Uses)
(apo; **detn.** of **nuclease activity** and use in **assays**)
IT Ligands
Receptors
RL: **ANT (Analyte)**; ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); **ANST (Analytical study)**; BIOL (Biological study); PROC (Process); USES (Uses)
(binding **assays**; **detn.** of **nuclease activity** and use in **assays**)
IT **Analysis**
(biochem.; **detn.** of **nuclease activity** and use in **assays**)
IT Nucleic acid hybridization
Test **kits**
(**detn.** of **nuclease activity** and use in **assays**)
IT **Immunoassay**
(enzyme; **detn.** of **nuclease activity** and use in **assays**)
IT Onium compounds
RL: ARG (Analytical reagent use); **ANST (Analytical study)**; USES (Uses)
(**tetrazolium**, dyes; **detn.** of **nuclease activity** and use in **assays**)
IT 9026-81-7, **Nuclease**
RL: **ANT (Analyte)**; **ANST (Analytical study)**
(**detn.** of **nuclease activity** and use in **assays**)
IT 54576-84-0, **Nuclease** P1
RL: **ANT (Analyte)**; BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **ANST (Analytical study)**; BIOL (Biological study)
(**detn.** of **nuclease activity** and use in **assays**)
IT 79-14-1, uses 100-63-0, Phenylhydrazine 50443-29-3 96602-60-7
RL: ARG (Analytical reagent use); **ANST (Analytical study)**; USES (Uses)
(**detn.** of **nuclease activity** and use in **assays**)
IT 9013-05-2, Phosphatase 9028-71-1D, Glycolate oxidase, apo 9031-66-7, Transaminase 9031-72-5, Alcohol dehydrogenase 9035-82-9, Dehydrogenase 9079-67-8, **Diaphorase**
RL: ARG (Analytical reagent use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **ANST (Analytical study)**; BIOL (Biological study); USES (Uses)
(**detn.** of **nuclease activity** and use in **assays**)
IT **50-89-5D**, **Thymidine**, derivs., reactions **53-84-9**, **NAD 58-61-7D**, **Adenosine**, derivs., reactions **58-68-4**, **NADH 58-96-8D**, **Uridine**, derivs. **71-30-7D**, **Cytosine**, derivs.

73-40-5D, Guanine, derivs. 288576-32-9D, derivs.
RL: ARG (Analytical reagent use); RCT (Reactant); **ANST (Analytical study)**; RACT (Reactant or reagent); USES (Uses)
(**detn.** of **nuclease activity** and use in **assays**)
IT 504-65-4, Formazan
RL: ARU (Analytical role, unclassified); FMU (Formation, unclassified); **ANST (Analytical study)**; FORM (Formation, nonpreparative)
(**detn.** of **nuclease activity** and use in **assays**)
IT 146-17-8, **Riboflavin** 5'-phosphate
RL: **ANT (Analyte)**; ARU (Analytical role, unclassified); FMU (Formation, unclassified); **ANST (Analytical study)**; FORM (Formation, nonpreparative)
(release and **detection** of; **detn.** of **nuclease activity** and use in **assays**)
IT 54-47-7, **Pyridoxal** phosphate 136-09-4, Thiamine **pyrophosphate** 529-96-4, **Pyridoxamine** phosphate
RL: ARU (Analytical role, unclassified); FMU (Formation, unclassified); **ANST (Analytical study)**; FORM (Formation, nonpreparative)
(release and **detection** of; **detn.** of **nuclease activity** and use in **assays**)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:260586 HCAPLUS
DOCUMENT NUMBER: 132:275154
TITLE: Detection of transcription factor activity by detection of nucleic acid nicking
INVENTOR(S): Hoeffler, Warren
PATENT ASSIGNEE(S): Xgene Corporation, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000022167	A1	20000420	WO 1999-US23277	19991006
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2346364	AA	20000420	CA 1999-2346364	19991006
AU 9961695	A1	20000501	AU 1999-61695	19991006
EP 1117830	A1	20010725	EP 1999-948532	19991006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527080	T2	20020827	JP 2000-576057	19991006

PRIORITY APPLN. INFO.: US 1998-103803P P 19981009
WO 1999-US23277 W 19991006

AB Certain transcription factors (enhancer binding proteins) significantly

increase transcription rates from genes by nicking a single DNA strand in the vicinity of their DNA binding sites, thereby allowing RNA polymerase to gain access to the transcribed DNA strand by a process of "threading". DNA template nicking is a detectable and quantifiable byproduct indicative of transcriptional activation that can be used to design practical assays. These assays are used to det. which transcription factors (enhancer binding proteins) are actively catalyzing the transcription of a gene in any cell type, or in any cell in response to any drug or treatment. Thus, TFIII, c-Jun, and CREB were found to create single-strand nicks in the DNA to which they are bound. The nicked and non-nicked DNA were separable by electrophoresis.

IC ICM C12Q001-68
CC 3-1 (Biochemical Genetics)
IT Transcription factors
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(CREB (cAMP-responsive element-**binding**); **detection** of transcription factor activity by **detection** of nucleic acid nicking)
IT **37288-25-8**, S1 **Nuclease**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(detection of transcription factor **activity** by detection of nucleic acid nicking)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:595421 HCAPLUS
DOCUMENT NUMBER: 131:224452
TITLE: Nucleic acid detection using a primer pyrophosphorylation/pyrophosphorolysis system
INVENTOR(S): Shultz, John W.; Manrekar, Michelle A.; Leippe, Donna M.; Lewis, Martin K.; Nelson, Lisa S.
PATENT ASSIGNEE(S): Promega Corporation, USA
SOURCE: PCT Int. Appl., 167 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9946409	A1	19990916	WO 1999-US5304	19990311
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6335162	B1	20020101	US 1998-42287	19980313
US 6159693	A	20001212	US 1999-252436	19990218
CA 2322797	AA	19990916	CA 1999-2322797	19990311
AU 9930792	A1	19990927	AU 1999-30792	19990311
EP 1064400	A1	20010103	EP 1999-912413	19990311
R: CH, DE, FR, GB, IT, LI, SE				
JP 2002505889	T2	20020226	JP 2000-535775	19990311

WO 2000049181 A1 20000824 WO 2000-US4243 20000218
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1155150 A1 20011121 EP 2000-908726 20000218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1998-42287 A2 19980313
US 1999-252436 A 19990218
WO 1999-US5304 W 19990311
US 1999-358972 A 19990727
US 1999-406064 A 19990927
WO 2000-US4243 W 20000218

AB This invention discloses methods for detecting specific nucleic acid sequences, interrogating the identity of a specific base within a sequence, and assaying endonuclease and exonuclease activity. DNA or RNA probes are hybridized to target nucleic acid sequences. Probes that are complementary to the target sequence at each base are depolymd., while probes which differ from the target at the interrogation position are not depolymd. The nucleic acid detection systems utilize the pyrophosphorolysis reaction catalyzed by various polymerases to produce deoxyribonucleoside triphosphates or ribonucleoside triphosphates, and the dNTPs are transformed to ATP by the action of nucleoside diphosphate kinase. The ATP produced by these reactions is detected by luciferase or NADH based detection systems.

IC ICM C12Q001-68
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 7, 9
ST nucleic acid **detection** primer pyrophosphorylation system; **nuclease detection** primer pyrophosphorylation system; exonuclease **detection** primer pyrophosphorylation system; endonuclease **detection** primer pyrophosphorylation; polyadenylate RNA **detection** pyrophosphorylation system
IT Mutation
Nucleic acid hybridization
Plasmids
Test **kits**
(nucleic acid detection using a primer pyrophosphorylation/pyrophosphorolysis system)
IT 9026-81-7, **Nuclease** 9055-11-2, Endonuclease 37228-74-3, Exonuclease
RL: **ANT (Analyte)**; **ANST (Analytical study)**
(nucleic acid **detection** using a primer pyrophosphorylation/pyrophosphorolysis system)
IT **58-68-4**, **NADH** 9012-90-2, DNA polymerase 9014-00-0, Luciferase 9015-83-2, PRPP synthase 9026-30-6, Poly(A) polymerase 9026-50-0, Nucleoside monophosphate kinase 9026-51-1, Nucleoside diphosphate kinase 9031-82-7, Phosphoribosylpyrophosphate transferase 9037-17-6, Nucleic acid polymerase 9068-38-6, Reverse transcriptase
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(nucleic acid detection using a primer pyrophosphorylation/pyrophosphorolysis system)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:100743 HCAPLUS
DOCUMENT NUMBER: 130:121849
TITLE: Graphitic nanotubes in luminescence **assays**
INVENTOR(S): Massey, Richard J.; Martin, Mark T.; Dong, Liwen; Lu, Ming; Fischer, Alan; Jameison, Fabian; Liang, Pam; Hoch, Robert; Leland, Jonathan K.
PATENT ASSIGNEE(S): Meso Scale Technology, USA
SOURCE: U.S., 42 pp., Cont.-in-part of U.S. Ser. No. 352,400. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5866434	A	19990202	US 1996-611347	19960306
US 6203814	B1	20010320	US 1994-352400	19941208
CA 2207282	AA	19960613	CA 1995-2207282	19951208
ZA 9701915	A	19970909	ZA 1997-1915	19970305
CA 2248893	AA	19970912	CA 1997-2248893	19970305
WO 9733176	A1	19970912	WO 1997-US3653	19970305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9720737	A1	19970922	AU 1997-20737	19970305
AU 724509	B2	20000921		
EP 885393	A1	19981223	EP 1997-908967	19970305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1217791	A	19990526	CN 1997-194334	19970305
JP 2001507787	T2	20010612	JP 1997-531989	19970305
US 6362011	B1	20020326	US 1999-243215	19990202
US 2002086335	A1	20020704	US 2001-7526	20011205

PRIORITY APPLN. INFO.:

US 1994-352400	A2	19941208
US 1996-611347	A	19960306
WO 1997-US3653	W	19970305
US 1999-243215	A1	19990202

AB Graphitic nanotubes, which include tubular fullerenes (commonly called "buckytubes") and fibrils, which are functionalized by chem. substitution, are used as solid supports in electrogenerated chemiluminescence assays. The graphitic nanotubes are chem. modified with functional group biomols. prior to use in an assay. Assocn. of electrochemiluminescent ruthenium complexes with the functional group biomol.-modified nanotubes permits detection of mols. including nucleic acids, antigens, enzymes, and enzyme substrates by multiple formats.

IC ICM G01N033-551
ICS G01N033-573; C12Q001-32; C12Q001-37
NCL 436526000
CC 9-5 (Biochemical Methods)
Section cross-reference(s): 3, 7, 15, 73, 80
ST graphitic nanotube electrochemiluminescence binding **assay**; tubular fullerene nanotube support electrochemiluminescence **assay** ; biosensor electrochemiluminescence carbon nanotube; **immunoassay** electrochemiluminescence graphitic nanotube; ruthenium complex

electrochemiluminescence graphitic nanotube
IT Separation
(affinity; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)
IT Nanotubes
Nanotubes
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(carbon fibers; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)
IT Nanotubes
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(carbon; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)
IT Optical detectors
(chemiluminescence, electro-; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)
IT Proteins, specific or class
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(conjugates, graphitic nanotube conjugates; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)
IT Luminescence, chemiluminescence
(detectors, electro-; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)
IT Chemiluminescence spectroscopy
(electro-; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)
IT **Immunoassay**
Luminescence, chemiluminescence
(electrochemiluminescence; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)
IT Biosensors
(enzymic; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)
IT Avidins
Polyoxyalkylenes, preparation
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(graphitic nanotube conjugates; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)
IT Biochemical molecules
Biosensors
Biotinylation
Electrochemical cells
Electrodes
Electrolytes, biological
Immobilization, biochemical
Luminescence
Luminescence spectroscopy
Magnetic field
Magnetic materials
Nucleic acid hybridization
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)
IT Antigens
Biopolymers
Nucleic acids
Oligonucleotides

Probes (nucleic acid)
RL: ANT (Analyte); ANST (Analytical study)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT DNA
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Fullerenes
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Enzymes, analysis
RL: ARU (Analytical role, unclassified); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Coenzymes
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Antibodies
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(immobilized; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(monoclonal; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Carbon fibers, reactions
Carbon fibers, reactions
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(nanotube; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 64-17-5, Ethanol, analysis 9001-40-5, Glucose 6-phosphate dehydrogenase 9001-62-1, Lipase 9002-07-7, Trypsin 9004-07-3, Chymotrypsin 9026-81-7, **Nuclease** 9032-92-2, Glycosidase 9035-82-9, Dehydrogenase
RL: **ANT (Analyte); ANST (Analytical study)**
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 196706-39-5P 196706-40-8P
RL: ANT (Analyte); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 7440-18-8D, Ruthenium, complexes, uses 9031-72-5, Alcohol dehydrogenase

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 9001-37-0, Glucose oxidase
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 15158-62-0
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 541-59-3DP, Maleimide, graphitic nanotube conjugates 5591-94-6P 196706-38-4P
RL: ARG (Analytical reagent use); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 52-90-4DP, L-Cysteine, graphitic nanotube conjugates **53-84-9DP**, **NAD**, analogs, graphitic nanotube conjugates 56-45-1DP, L-Serine, graphitic nanotube conjugates 56-84-8DP, L-Aspartic acid, graphitic nanotube conjugates 56-86-0DP, L-Glutamic acid, graphitic nanotube conjugates 60-18-4DP, L-Tyrosine, graphitic nanotube conjugates 72-19-5DP, L-Threonine, graphitic nanotube conjugates 107-15-3DP, 1,2-Ethanediamine, graphitic nanotube conjugates, preparation 9013-20-1DP, Streptavidin, graphitic nanotube conjugates 15746-57-3DP, graphitic nanotube conjugates 25322-68-3DP, graphitic nanotube conjugates 196706-41-9DP, graphitic nanotube conjugates 196706-42-0DP, graphitic nanotube conjugates
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 2418-95-3 13139-17-8 196706-37-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 2389-60-8P 128972-27-0P 196706-37-3DP, amide protecting group terminated
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 7440-44-0, Carbon, reactions
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(nanotubes; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:806816 HCAPLUS
DOCUMENT NUMBER: 130:48291
TITLE: method for highly sensitive nucleic acid detection with Imprint primers for single copy detection
INVENTOR(S): Creighton, Steven; Gold, Larry

PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9855653	A1	19981210	WO 1998-US11457	19980603
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9878136	A1	19981221	AU 1998-78136	19980603

PRIORITY APPLN. INFO.:		
US 1997-48886P	P	19970606
US 1998-27107	A	19980220
WO 1998-US11457	W	19980603

AB A novel method for the highly selective detection of a specific target nucleic acid sequence in a sample compn. that may contain a large no. of nucleic acids. A copy of a target nucleic acid sequence is first formed by extension from a first primer complementary to part of the target sequence. A hybrid is then formed between this copy of the target nucleic acid sequence and a second primer, and the detection of the target nucleic acid sequence is based on the formation of pyrophosphate and/or dNMP. The embodiments all involve the establishment of Idling conditions using a hybrid formed between the target nucleic acid and one or more probe primer. The net result of the Idling phenomenon is the prodn. of dNMP and PPi. Imprint primers are described that synthesize a copy, or Imprint, of the target nucleic acid that highly increase the specificity of the technique. These imprint primers are wholly or partly comprised of nuclease resistant nucleic acid residues and labeled with a group such as biotin which permits subsequent attachment to a solid support. This primer is chosen so that it hybridizes to the target nucleic acid at a position that is 3' to the location of the sequences that will later be used for Idling establishment. Trapping of Imprint and elimination of non-imprint nucleic acids is performed using avidin-coated paramagnetic beads binding to biotin. The creation of a solid phase support-bound imprint can drastically reduce the complexity of the sample. Target nucleic acid detection is indicated by PPi or NADH or ATP measured in fluormetric or electrochem. or light anal. assays. The methods have the potential to detect a single copy a target nucleic acid.

IC ICM C12Q001-68
CC 3-1 (Biochemical Genetics)
IT Electrochemical analysis
(Electrochem. anal. detecting **NADH** indicating target detection; method for highly sensitive nucleic acid detection with Imprint primers for single copy detection)
IT Fluorometry
(Fluorometry detecting **NADH** indicating target detection; method for highly sensitive nucleic acid detection with Imprint primers for single copy detection)
IT Coenzymes
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**NADH** amplification by coenzyme cycling; method for highly sensitive nucleic acid detection with Imprint primers for single copy detection)

IT Light
(detecting **NADH** indicating target detection; method for highly sensitive nucleic acid detection with Imprint primers for single copy detection)

IT 60-92-4, Cyclic Amp 485-84-7, **Adenosine** 5'-phosphosulfate 2140-58-1, ADP-glucose 24937-83-5, Polyadenosine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ATP generation indicating target nucleic acid detection and prodn. utilizing; method for highly sensitive nucleic acid detection with Imprint primers for single copy detection)

IT 9055-15-6, Oxidoreductase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**NADH** generation in bacterial luciferase system comprising oxidoreductase; method for highly sensitive nucleic acid detection with Imprint primers for single copy detection)

IT 9014-00-0, Luciferase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**NADH** generation in bacterial luciferase system; method for highly sensitive nucleic acid detection with Imprint primers for single copy detection)

IT 9026-81-7, **Nuclease**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(generation of target sequence resistant to; method for highly sensitive nucleic acid **detection** with Imprint primers for single copy **detection**)

IT 58-98-0, **Uridine**-5'-diphosphate, biological studies 146-17-8, Fmn 9001-81-4, Phosphoglucomutase 9012-39-9, Atp sulfurylase 9030-27-7
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(nucleic acid detection involving PPi detection involving; method for highly sensitive nucleic acid detection with Imprint primers for single copy detection)

IT 14000-31-8, **Pyrophosphate**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(target nucleic acid detection by **NADH** generation or PPi utilizing enzymically-cleaved intermediates; method for highly sensitive nucleic acid detection with Imprint primers for single copy detection)

IT **53-84-9**, **Nad** 56-73-5, Glucose 6-phosphate 59-56-3 133-89-1, **Uridine**-5'-diphosphate-glucose 9001-40-5, Glucose-6-phosphate dehydrogenase 9026-22-6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(target nucleic acid detection by **NADH** generation utilizing enzymically-cleaved intermediates; method for highly sensitive nucleic acid detection with Imprint primers for single copy detection)

IT **58-68-4**, **Nadh** 2466-09-3, Diphosphoric acid
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(target nucleic acid detection indicated by formation of; method for highly sensitive nucleic acid detection with Imprint primers for single

copy detection)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:618265 HCAPLUS
DOCUMENT NUMBER: 127:275017
TITLE: Graphitic nanotubes in luminescence **assays**
INVENTOR(S): Massey, Richard J.; Martin, Mark T.; Dong, Liwen; Lu, Ming; Fischer, Alan; Jameison, Fabian; Liang, Pam; Hoch, Robert; Leland, Jonathon K.
PATENT ASSIGNEE(S): Igen, Inc., USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9733176	A1	19970912	WO 1997-US3653	19970305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5866434	A	19990202	US 1996-611347	19960306
AU 9720737	A1	19970922	AU 1997-20737	19970305
AU 724509	B2	20000921		
EP 885393	A1	19981223	EP 1997-908967	19970305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001507787	T2	20010612	JP 1997-531989	19970305

PRIORITY APPLN. INFO.: US 1996-611347 A 19960306
US 1994-352400 A2 19941208
WO 1997-US3653 W 19970305

AB Graphitic nanotubes, which include tubular fullerenes (commonly called "buckytubes") and fibrils, which are functionalized by chem. substitution, are used as solid supports in electrogenerated chemiluminescence assays. The graphitic nanotubes are chem. modified with functional group biomols. prior to use in an assay. Assocn. of electrochemiluminescent ruthenium complexes with the functional group biomol.-modified nanotubes permits detection of mols. including nucleic acids, antigens, enzymes, and enzyme substrates by multiple formats.

IC ICM G01N033-573
ICS G01N033-553; C07K016-44

CC 9-5 (Biochemical Methods)
Section cross-reference(s): 3, 7, 15, 73, 80

ST graphitic nanotube electrochemiluminescence binding **assay**; tubular fullerene nanotube support electrochemiluminescence **assay**; biosensor electrochemiluminescence carbon nanotube; **immunoassay** electrochemiluminescence graphitic nanotube; ruthenium complex electrochemiluminescence graphitic nanotube

IT Separation
(affinity; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Nanotubes
Nanotubes
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(carbon fibers; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Nanotubes
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(carbon; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Optical detectors
(chemiluminescence, electro-; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Luminescence, chemiluminescence
(detectors, electro-; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Chemiluminescence spectroscopy
(electro-; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT **Immunoassay**
(electrochemiluminescence; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Biosensors
(enzymic; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Avidins
Polyoxyalkylenes, preparation
Proteins, general, preparation
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(graphitic nanotube conjugates; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Biochemical molecules
Biosensors
Biotinylation
Electrochemical cells
Electrodes
Electrolytes, biological
Immobilization, biochemical
Luminescence spectroscopy
Magnetic field
Magnetic materials
Nucleic acid hybridization
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Antigens
Biopolymers
Nucleic acids
Oligonucleotides
Probes (nucleic acid)
RL: ANT (Analyte); ANST (Analytical study)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Fullerenes
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);

RACT (Reactant or reagent); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Antibodies
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(immobilized; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(monoclonal; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT Carbon fibers, reactions
Carbon fibers, reactions
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(nanotube; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 64-17-5, Ethanol, analysis 9001-40-5, Glucose 6-phosphate dehydrogenase 9001-62-1, Lipase 9002-07-7, Trypsin 9004-07-3, Chymotrypsin 9026-81-7, **Nuclease** 9032-92-2, Glycosidase 9035-82-9, Dehydrogenase
RL: **ANT (Analyte); ANST (Analytical study)**
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 196706-39-5P 196706-40-8P
RL: ANT (Analyte); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 7440-18-8D, Ruthenium, complexes, uses 9031-72-5, Alcohol dehydrogenase
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 9001-37-0, Glucose oxidase
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 15158-62-0
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 541-59-3DP, Maleimide, graphitic nanotube conjugates 5591-94-6P 196706-38-4P
RL: ARG (Analytical reagent use); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 52-90-4DP, L-Cysteine, graphitic nanotube conjugates, preparation
53-84-9DP, NAD, analogs, graphitic nanotube conjugates
56-45-1DP, L-Serine, graphitic nanotube conjugates, preparation
56-84-8DP, L-Aspartic acid, graphitic nanotube conjugates, preparation
56-86-0DP, L-Glutamic acid, graphitic nanotube conjugates, preparation
60-18-4DP, L-Tyrosine, graphitic nanotube conjugates, preparation
72-19-5DP, L-Threonine, graphitic nanotube conjugates, preparation
107-15-3DP, 1,2-Ethanediamine, graphitic nanotube conjugates, preparation

9013-20-1DP, Streptavidin, graphitic nanotube conjugates 15746-57-3DP, graphitic nanotube conjugates 25322-68-3DP, graphitic nanotube conjugates 196706-41-9DP, graphitic nanotube conjugates 196706-42-0DP, graphitic nanotube conjugates
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 2418-95-3 13139-17-8 196706-37-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 2389-60-8P 128972-27-0P 196706-37-3DP, amide protecting group terminated
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

IT 7440-44-0, Carbon, reactions
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(nanotubes; graphitic nanotubes in luminescence **assays** of biomols. and biopolymers)

L56 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:628580 HCAPLUS
DOCUMENT NUMBER: 125:267507
TITLE: Method of distinguishing between neoplasms and pseudoneoplastic or hyperplastic processes by restrictase digestion of polymorphic X chromosome gene and heteroduplex generation
INVENTOR(S): Stoerker, Jay; Shroyer, Kenneth R.
PATENT ASSIGNEE(S): Avitech Diagnostics, Inc., USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9627024	A1	19960906	WO 1996-US2311	19960301
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5843649	A	19981201	US 1995-396927	19950301
AU 9651714	A1	19960918	AU 1996-51714	19960301

PRIORITY APPLN. INFO.: US 1995-396927 19950301
WO 1996-US2311 19960301

AB Methods of distinguishing between neoplasms and pseudoneoplastic or hyperplastic processes are disclosed. The methods comprise first contacting DNA from cells of a tissue sample from a female individual with a cytosine methylation-specific endonuclease, generating amplified fragments of a cytosine methylation-regulatable polymorphic X chromosome gene using primers that bracket a restriction site of said cytosine methylation-specific endonuclease and a polymorphic sequence in said nucleotide sequence of the gene; generating heteroduplexes between amplified fragments and heteroduplex generators which consist of 1-5 nucleotide differences from the amplified fragments; and detecting the presence of a single species of heteroduplex or two species of

heteroduplexes. THe presence of a single species of heteroduplex which indicates amplified fragments from a clonal population of cells which is indicative of a neoplasm and the presence of two species of heteroduplexes indicates amplified fragments from a mosaic population of cells is indicative a pseudoneoplastic or hyperplastic process. Reagents and kits for performing the methods are disclosed.

IC ICM C12Q001-68
ICS C12P019-34; C07H021-04

CC 3-1 (Biochemical Genetics)

ST neoplasm pseudoneoplastic hyperplastic cell **assay**; restrictase X chromosome inactivation cancer diagnosis; methylation RFLP X chromosome cancer diagnosis

IT Gene, animal
RL: ANT (Analyte); ANST (Analytical study)
(**cytosine** methylation-regulatable polymorphic; method of distinguishing between neoplasms and pseudoneoplastic or hyperplastic processes by restrictase digestion of polymorphic X chromosome gene and heteroduplex generation)

IT 9075-08-5, **Nuclease**, restriction endodeoxyribo-
RL: ARG (Analytical reagent use); **ANST (Analytical study)**; USES (Uses)
(**cytosine** methylation-specific; method of distinguishing between neoplasms and pseudoneoplastic or hyperplastic processes by restrictase digestion of polymorphic X chromosome gene and heteroduplex generation)

IT 81295-25-2, **Nuclease**, restriction endodeoxyribo-, HpaII
RL: ARG (Analytical reagent use); **ANST (Analytical study)**; USES (Uses)
(method of distinguishing between neoplasms and pseudoneoplastic or hyperplastic processes by restrictase digestion of polymorphic X chromosome gene and heteroduplex generation)

L56 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:578847 HCAPLUS
DOCUMENT NUMBER: 115:178847
TITLE: Enzyme **assay** and **assay kit** to measure cellular activation
INVENTOR(S): Jaffe, Russell M.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9106859	A1	19910516	WO 1990-US6214	19901025
W: AU, BG, BR, CA, FI, HU, JP, KR, NO, SU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2070408	AA	19910426	CA 1990-2070408	19901025
CN 1051791	A	19910529	CN 1990-109600	19901025
AU 9066474	A1	19910531	AU 1990-66474	19901025
EP 497870	A1	19920812	EP 1990-916544	19901025
EP 497870	B1	19980916		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05502099	T2	19930415	JP 1990-515678	19901025
JP 3014752	B2	20000228		
AT 171277	E	19981015	AT 1990-916544	19901025

ES 2121756 T3 19981216 ES 1990-916544 19901025
PRIORITY APPLN. INFO.: US 1989-426294 A 19891025
WO 1990-US6214 A 19901025

AB An assay for detecting the response or activation of cells, including lymphocytes, and a method for detecting immunol. sensitization in a subject, involve the introduction of a cell-activating substance which causes an enzyme of the cells to become available for reaction and then measurement of the enzymic reaction using a substrate which generates a detectable product. A kit for detecting cell activation comprises cell-activating substances, an enzyme substrate, a support matrix, and reaction vessels, esp. a microtitration plate. Aliquots of cell-rich plasma and tetrazolium blue (enzyme substrate) were transferred to virgin optical styrene 48-well microtiter plates to which various food and chem. antigens had been previously attached. The cells were incubated at 35.degree. for 3 h and absorbance was read at 340 nm or 340-380 nm. Enzyme activation was obsd. both as an increase in apparent cell vol. and as a fall in absorbance of the incubation medium. The assay permitted consistent quant. assessment of foods and chems. that cause immunol. hypersensitivity reactions in sensitive individuals.

IC ICM G01N033-53
ICS C12Q001-00; B01L003-00
CC 9-2 (Biochemical Methods)
Section cross-reference(s): 7, 15, 17
ST enzyme **assay** cell activation; lymphocyte activation enzyme **assay**; immunol hypersensitivity food chem spectrophotometry

IT Basophil
Blood corpuscle
Eukaryote
Monocyte
Prokaryote
(activation of, by enzyme **assay**)

IT Animal cell
Lymphocyte
(activation of, detn. of, by enzyme **assay**)

IT Glutens
RL: ANST (Analytical study)
(as cell-activating substance in enzyme **assay** of cell activation or immunol. sensitization)

IT Allergens
Glycopeptides
Haptens
Lipoproteins
Peptides, biological studies
RL: ANST (Analytical study)
(as cell-activating substances in enzyme **assay** of cell activation or immunol. sensitization)

IT Blood analysis
(immunol. sensitization detn. in, by enzyme **assay**)

IT Agglutinins and Lectins
RL: ANST (Analytical study)
(phytohemagglutinins, as cell-activating substance in enzyme **assay** of cell activation or immunol. sensitization)

IT 14265-45-3, Sulfite
RL: ANST (Analytical study)
(as cell-activating substance in enzyme **assay** of cell activation or immunol. sensitization)

IT 298-95-3, Neotetrazolium 1871-22-3, **Tetrazolium** blue
RL: ANST (Analytical study)
(as substrate for enzyme detn. in detn. of cell activation or immunol. sensitization)

IT 407-41-0 7665-99-8, Cyclic **guanosine** monophosphate
21820-51-9, Phosphotyrosine 56-65-5, **Adenosine** triphosphate, biological studies 58-64-0, **Adenosine** diphosphate, biological studies 60-92-4 146-91-8, **Guanosine** diphosphate
RL: ANST (Analytical study)
(as substrate for kinase detn. in detn. of cell activation or immunol. sensitization)
IT 24936-38-7 24939-03-5
RL: **ANST (Analytical study)**
(as substrate for **nuclease detn.** in **detn.** of cell activation or immunol. sensitization)
IT 9001-62-1, Lipase 9013-05-2, Phosphatase 9026-81-7, **Nuclease** 9027-41-2, Hydrolase 9027-52-5, Hexosaminidase 9031-44-1, Kinase 9031-96-3, Peptidase
RL: **ANT (Analyte); ANST (Analytical study)**
(**detn.** of, in **detn.** of cell activation or immunol. sensitization)

L56 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:135617 HCAPLUS
DOCUMENT NUMBER: 112:135617
TITLE: A **kit** and monoclonal antibodies in detection of cell surface receptors and of halodeoxyuridines taken up by cells during DNA synthesis
INVENTOR(S): Evans, Elizabeth L.; Gonchoroff, Nick J.; Greipp, Philip R.; Houck, David W.; Katzmann, Jerry A.; Kyle, Robert A.; Loken, Michael R.
PATENT ASSIGNEE(S): Becton, Dickinson and Co., USA
SOURCE: U.S., 11 pp. Cont. of U.S. Ser. No. 798,506, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4885237	A	19891205	US 1988-205013	19880606

PRIORITY APPLN. INFO.: US 1985-798506 19851115

AB Halodeoxyuridines (halodu) taken up by cells during DNA synthesis and cell surface receptors are detected by monoclonal antibodies. A diagnostic kit for detecting the DNA comprises an anti-halodu monoclonal antibody and an enzyme capable of partially disrupting the H bonds between the DNA strands to expose the incorporated halodu. Lymphocytes from a normal donor were incubated for 72 h in RPM1 1640 supplemented with PHA. 5-Bromo-2-deoxyuridine (BrdU) was added during the final 6 h and the cells were treated with colcemid for 1 h prior to harvesting. Bu-1 antibody (monoclonal antibody to halodu) and nuclease from Mycoplasma fermentans were added and bound antibody was detected using fluorescent microscopy by the addn. of FITC-labeled goat antimouse IgG conjugate. Control slides with the monoclonal antibody or conjugate alone were neg.

IC ICM C12Q001-68
ICS G01N033-00
NCL 435006000
CC 9-10 (Biochemical Methods)
ST monoclonal antibody halodeoxyuridine cell DNA detection; bromodeoxyuridine monoclonal antibody lymphocyte DNA detection; **uridine** halodeoxy monoclonal antibody cell DNA; surface receptor cell DNA detection antibody
IT Microorganism

Mycoplasma fermentans
Pancreas, composition
(**nuclease** of, in **detection** of halodeoxyuridine incorporation in cellular DNA by monoclonal antibodies)
IT 9003-98-9, DNase 9026-81-7, **Nuclease**
RL: **ANST (Analytical study)**
(in **detection** of halodeoxyuridine incorporation in cellular DNA by monoclonal antibodies)

L56 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:34504 HCAPLUS
DOCUMENT NUMBER: 108:34504
TITLE: **Kits** and procedures for enzymic labeling of nucleotide triphosphates with 32P or 35S in the .alpha., .beta., or .gamma. positions
INVENTOR(S): Brahms, Georges; Dargouse, Olivier; Quagliaroli, Daniel; Vergne, Jacques; Bardy, Andre
PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique, Fr.
SOURCE: Fr. Demande, 26 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2585724	A1	19870206	FR 1985-11795	19850801
FR 2585724	B1	19881014		
EP 214014	A1	19870311	EP 1986-401701	19860730
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 62044196	A2	19870226	JP 1986-181807	19860801

PRIORITY APPLN. INFO.: FR 1985-11795 19850801

AB A kit and method for nucleoside-nonspecific enzymic prepn. of deoxyribo- and ribonucleotide triphosphates (dNTP, NTP) or their derivs. labeled in the .alpha., .beta., or .gamma. position with [32P]-orthophosphate or [35S]-thiophosphate comprise (a) a means to fix a labeled phosphate onto 5'-NDP in the .gamma. position; (b) a means to displace the .gamma. phosphoryl group of 5'-NTP onto the 5' position of a 3'-NMP; (c) a means to dephosphorylate the 3' phosphate of the 5',3'-NDP; (d) a means to fix 2 phosphates at the 5' position of 5'-NMP; and (e) a means to displace the labeled phosphoryl group of 5'-NTP onto a 5'-NMP at the .beta. position and phosphorylating the resultant 5'-NDP. [.beta.-32P]ATP was prepd. by reacting 48 .mu.L enzyme compn. 1 contg. glycerol-3-phosphate dehydrogenase 70, triose phosphate isomerase 0.7, glyceraldehyde-3-phosphate dehydrogenase 70, 3-phosphoglycerate kinase 34.5, lactate dehydrogenase 34.5 .mu.g/mL, Tris-HCl (pH 9) 105, MgCl2 25, dithiotreitol (DTT) 12.5, spermine 4, L-glycerophosphate 0.3, NAD 1, and Na pyruvate 2 mM with 2 .mu.L 2.5 mM 5'-UDP and 50 .mu.L H3[32P]PO4 at 23.degree. for 1.5 h; heating the soln. for 2 min at 90.degree.; and doubling the vol. by addn. of enzyme compn. 2 contg. pyruvate kinase 600, NMP kinase 2500, NDP kinase 510 .mu.g/mL, Tris-HCl (pH 8-7.8) 50, MgCl2 10, DTT 5, KCl 4, and PEP 4 mM and reacting with 2 .mu.L 2.5 mM 5'-AMP for .apprx.3.5 h.

IC ICM C12P019-40
ICS C12P019-38; C07H019-10; C07H019-20
CC 9-8 (Biochemical Methods)
Section cross-reference(s): 33
IT **53-84-9**, **NAD** 57-03-4 113-24-6, Sodium pyruvate
138-08-9, PEP 9001-50-7, Glyceraldehyde-3-phosphate dehydrogenase
9001-59-6, Pyruvate kinase 9001-60-9, Lactate dehydrogenase 9001-83-6,

3-Phosphoglycerate kinase 9023-78-3, Triosephosphate isomerase
9026-50-0 9026-51-1 9075-65-4, Glycerol-3-phosphate dehydrogenase
37211-65-7 54576-84-0, **Nuclease** P1
RL: **ANST (Analytical study)**
(enzyme compns. contg., for radiolabeling nucleotide triphosphates)

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    http://www.derwent.com/userguides/dwpi_guide.html <<<

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     (FILE 'WPIDS' ENTERED AT 11:24:11 ON 09 DEC 2002)
               DEL HIS Y

     FILE 'STNGUIDE' ENTERED AT 11:28:28 ON 09 DEC 2002

     FILE 'WPIDS' ENTERED AT 11:34:51 ON 09 DEC 2002
L1          1232 S NUCLEASE#
L2         10696 S NUCLEOSID? OR CYTIDINE OR ADENOSINE OR GUANOSINE OR THYMIDINE
L3         15122 S L2 OR NICOTINAMIDE OR NAD OR NADH OR NAD3P OR NAD3PH
L4           204 S L1 AND  L3
L5         26144 S KIT#
L6         34232 S ASSAY? OR IMMUNOASSAY?
L7            25 S L4 AND L5
L8            24 S L4 AND L6
L9            43 S L7 OR L8
                 E WO2000049172/PN
L11          372 S L1 (S) (DETN OR DETECT? OR DETERMIN? OR ANAL?)
L12           66 S L11 AND L3
L13           41 S APOENZYM?
L14            1 S L12 AND L13
L15            1 S DIOXETANE AND L12
L16         5945 S RIBOFLAVIN OR PYRIDOXAL OR PYRIDOXAMINE OR PYROPHOSPHATE#
L17            3 S L12 AND L16
L18         4528 S PHOSPHO RADICAL OR PROSTHETIC
L19            2 S L12 AND L18
L20         3806 S BIND? (3A) DETECT?
L21            7 S L12 AND L20
L22        26144 S KIT#
L23           11 S L12 AND L22
L24           10 S L14 OR L15 OR L17 OR L17 OR L19 OR L21
L25           14 S L12 AND L6
L26           20 S L23 OR L25
L27           23 S L26 OR L24
L28         4563 S TETRAZOLIUM OR DEHYDROGENASE# OR DIAPHORASE#
L29            3 S L12 AND L28
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L30          24 S L29 OR L27

     FILE 'WPIDS' ENTERED AT 11:54:59 ON 09 DEC 2002

=> d que l30
L1         1232 SEA FILE=WPIDS ABB=ON  PLU=ON  NUCLEASE#
L2        10696 SEA FILE=WPIDS ABB=ON  PLU=ON  NUCLEOSID? OR CYTIDINE OR
                ADENOSINE OR GUANOSINE OR THYMIDINE OR URIDINE
L3        15122 SEA FILE=WPIDS ABB=ON  PLU=ON  L2 OR NICOTINAMIDE OR NAD OR
                NADH OR NAD3P OR NAD3PH
L6        34232 SEA FILE=WPIDS ABB=ON  PLU=ON  ASSAY? OR IMMUNOASSAY?
L11         372 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (S) (DETN OR DETECT? OR
                DETERMIN? OR ANAL?)
L12          66 SEA FILE=WPIDS ABB=ON  PLU=ON  L11 AND L3
L13          41 SEA FILE=WPIDS ABB=ON  PLU=ON  APOENZYM?
L14           1 SEA FILE=WPIDS ABB=ON  PLU=ON  L12 AND L13
L15           1 SEA FILE=WPIDS ABB=ON  PLU=ON  DIOXETANE AND L12
L16        5945 SEA FILE=WPIDS ABB=ON  PLU=ON  RIBOFLAVIN OR PYRIDOXAL OR
                PYRIDOXAMINE OR PYROPHOSPHATE#
L17           3 SEA FILE=WPIDS ABB=ON  PLU=ON  L12 AND L16
L18        4528 SEA FILE=WPIDS ABB=ON  PLU=ON  PHOSPHO RADICAL OR PROSTHETIC
L19           2 SEA FILE=WPIDS ABB=ON  PLU=ON  L12 AND L18
L20        3806 SEA FILE=WPIDS ABB=ON  PLU=ON  BIND? (3A) DETECT?
L21           7 SEA FILE=WPIDS ABB=ON  PLU=ON  L12 AND L20
L22       26144 SEA FILE=WPIDS ABB=ON  PLU=ON  KIT#
L23          11 SEA FILE=WPIDS ABB=ON  PLU=ON  L12 AND L22
L24          10 SEA FILE=WPIDS ABB=ON  PLU=ON  L14 OR L15 OR L17 OR L17 OR L19
                OR L21
L25          14 SEA FILE=WPIDS ABB=ON  PLU=ON  L12 AND L6
L26          20 SEA FILE=WPIDS ABB=ON  PLU=ON  L23 OR L25
L27          23 SEA FILE=WPIDS ABB=ON  PLU=ON  L26 OR L24
L28        4563 SEA FILE=WPIDS ABB=ON  PLU=ON  TETRAZOLIUM OR DEHYDROGENASE#
                OR DIAPHORASE#
L29           3 SEA FILE=WPIDS ABB=ON  PLU=ON  L12 AND L28
L30          24 SEA FILE=WPIDS ABB=ON  PLU=ON  L29 OR L27


=> d .wp l30 1-24

L30  ANSWER 1 OF 24  WPIDS (C) 2002 THOMSON DERWENT
AN   2002-216734 [27]   WPIDS
DNC  C2002-066154
TI   Novel asynchronous thermal cycling method for amplification of target
     nucleic acid, involves two annealing and two extension steps employing two
     primers which differ in their thermal melting temperatures.
DC   B04 D16
IN   CHEN, C; EGHOLM, M; HAFF, L
PA   (APPL-N) APPLERA CORP
CYC  93
PI   WO 2001094638 A2 20011213 (200227)* EN   87p
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
            DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
            LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
            SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     AU 2001068235 A  20011217 (200229)
ADT  WO 2001094638 A2 WO 2001-US18464 20010606; AU 2001068235 A AU 2001-68235
     20010606
FDT  AU 2001068235 A Based on WO 200194638
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PRAI US 2001-875211 20010605; US 2000-209883P 20000606
AB WO 200194638 A UPAB: 20020429
NOVELTY - Amplifying nucleic acid (NA) by annealing primer (P1) to first strand (S1) of denatured target NA (dNA) at annealing temperature (T1); extending P1 at T1 or extension temperature (E1) to generate double-stranded (ds) NA; annealing primer (P2) to second strand (S2) of (dNA) at annealing temperature (T2), lower than (T1), (E1); extending P2 to generate dsNA; denaturing target dsNA into S1 and S2.

DETAILED DESCRIPTION - The above method comprises annealing P1 to S1 of a denatured target NA at first annealing temperature (T1); extending P1 with primer extension reagents at an extension temperature or T1 to generate a dsNA, where the reagents comprise a polymerase, nucleotide 5'-triphosphates and a buffer; annealing P2 to S2 of a denatured target NA at a second annealing temperature (T2) lower than T1 and extension temperature; extending P2 with primer extension reagents at the extension temperature to generate a dsNA; and denaturing the ds target NA into S1 and S2 at a denaturing temperature. A probe hybridization step may be incorporated into the cycle. A detectable probe is annealed to S2 of denatured target NA at a probe hybridization temperature.

INDEPENDENT CLAIMS are also included for the following:

(1) producing complementary polynucleotide strands of a target polynucleotide, by:

(a) obtaining a mixture comprising first and second target polynucleotide strands which are capable of hybridizing with each other to form a base-paired structure that contains a target sequence, P1 that is complementary to a first region in the first target polynucleotide strand, and P2 that is complementary to a second region in the second target polynucleotide strand, such that the first and second regions flank the target sequence;

(b) extending P1 at a first temperature to form a first complex comprising a first complementary strand that is hybridized to the first target strand, under conditions such that P2 does not substantially hybridize to the second region; and

(c) extending P2 at a second temperature that is lower than the first temperature, to form a second complex comprising a second complementary strand that is hybridized to the second target strand, where before extending P2, a detectable probe is hybridized to a complementary binding region in the second target strand, and the hybridized probe is detected as a measure of second target strand; and

(2) a **kit** for amplifying a target polynucleotide comprising two or more primers having a thermal melting point (Tm) different of 10-30 deg. C.

USE - The method is useful for amplifying target NA, preferably a plasmid, cDNA, amplicon, genomic DNA, restriction digest or a ligation product, or a target comprising single nucleotide polymorphisms (claimed). The asynchronous PCR cycle has utility in **nuclease** cleavage **assay** with a cleaving DNA fluorescence resonance energy transfer (FRET) probe, in **assays** for human disease diagnosis, food-borne pathogen **detection** and microbial **detection**, for allelic discrimination of target DNA, and in genotyping and gene expression **analysis**.

ADVANTAGE - Asynchronous PCR provides a significant advantage by efficient production of a single-stranded amplicon ready for hybridization and precluding amplicon isolation, denaturation and purification.

DESCRIPTION OF DRAWING(S) - The figure shows a schematic for an asynchronous PCR thermal cycling method.

Dwg.1/22

TECH UPTX: 20020429
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: P1 and P2 are DNA or peptide nucleic acid (PNA)/DNA chimera, and comprise a covalently attached

fluorescent dye, mobility-modifier or minor groove binder. The concentration of P1 is 2-10 times higher than concentration of P2. The steps are repeated for 2-50 cycles. The change in fluorescence intensity is detected at the end-point of target amplification, which indicates the presence of the target sequence and is monitored in real-time. T1 is 10-30degreesC, preferably 12-16degreesC higher than T2. T1 is preferably 60-75degreesC and T2 is 45-55degreesC. P1 has a (GC)n or (CG)n sequence at the 5' terminus, where n is 1-4. A label is covalently attached to one or more of the nucleotide 5'-triphosphates at the 8-C of a purine nucleobase, 7-C or 8-C of a 7-deazapurine nucleobase, or the 5-position of a pyrimidine nucleobase, or is attached to P1 or P2 at a 5' terminus, sugar, an internucleotide linkage, or a nucleobase. The step of annealing P2 to second strand of denatured target and extending P2 are omitted in the last 1-25 cycles, where a mixture of single-stranded and dsDNA is produced. Preferred Probe: The detectable probe includes a fluorescent moiety and a quencher moiety, which are attached to the 5' or 3' terminus of the probe. The probe is detected prior to extension of P2. The probe is (non)-enzymatically cleaved. The probe comprises a target-binding sequence and two intramolecularly base-paired sequences, and forms a hairpin stem and loop structure. The intramolecularly base-paired sequences are at the 5' and 3' terminus of the probe. The probe comprises one or more 2-aminoethylglycine (PNA) monomer units and is a PNA/DNA chimera. The probe has the structure (A).

R = fluorescent moiety such as fluorescein, rhodamine or cyanine dye;
L1 = a linker having one or more D or E amino acid residue;
L2 = a linker having one or more K amino acid residue;
B = uracil, thymine, cytosine, adenine, 7-deazaadenine, guanine, 7-deazaguanosine, 7-deaza-8-azaguanine or 7-deaza-8-azaadenine;
Q = quencher moiety such as rhodamine, nitro-substituted cyanine dye or has the structure (B) or (C);
n = 5-25;
Z = H, Cl, F, 1-6C alkyl, 5-14C aryl, nitro, cyano, sulfonate, NR2, -OR, CO2H; and
R = H, 1-6C alkyl or 5-14C aryl.

The probe comprises one or more nucleotide analogs chosen from a nucleobase analog, a 2'-deoxyribose analog, an internucleotide analog and an optical isomer. The nucleotide analog is a 2'-deoxyribose analog that is substituted at the 2'-carbon atom with Cl, F, -R, OR- or -NR2, where R is independently -H, 1-6C alkyl or 5-14C aryl. The nucleotide analog is an LNA, L-form optical isomer of 2'-deoxyribose. The nucleobase analog is 7-deazaadenine, 7-deazaguanine, 7-deaza-8-azaguanine, 7-deaza-8-azaadenine, inosine, nebularine, nitropyrrole, nitroindole, 2-amino-purine, 2,6-diamino-purine, hypoxanthine, pseudouridine, pseudocytidine, pseudoisocytidine, 5-propynyl-**cytidine**, isocytidine, isoguanine, 7-deaza-quanine, 2-thio-pyrimidine, 6-thio-guanine, 4-thio-thymine, 4-thio-uracil, O6-methyl-guanine, N6-methyl-adenine, O4-methyl-thymine, 5,6-dihydrothymine, 5,6-dihydrouracil, 4-methyl-indole and ethenoadenine. Preferred **Kit**: The **kit** further comprises polymerase, detectable probe and one or more enzymatically-extendable nucleotides.

L30 ANSWER 2 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-206219 [26] WPIDS
CR 2002-188733 [24]
DNN N2002-157036 DNC C2002-063239
TI Methods for detecting one or more non-nucleic acid analytes using fusion polypeptides with specificity for the analyte, where the polypeptide comprises first and second inactive functional domains and an analyte binding domain.
DC B04 D16 S03

IN DAVIS, S C; KREBBER, C; MINSHULL, J; RAILLARD, S A; VOGEL, K; WELCH, M
PA (MAXY-N) MAXYGEN INC
CYC 96
PI WO 2002010750 A2 20020207 (200226)* EN 159p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001079135 A 20020213 (200238)
US 2002127623 A1 20020912 (200262)
ADT WO 2002010750 A2 WO 2001-US24182 20010731; AU 2001079135 A AU 2001-79135 20010731; US 2002127623 A1 Provisional US 2000-222056P 20000731, Provisional US 2000-244764P 20001031, US 2001-920607 20010731
FDT AU 2001079135 A Based on WO 200210750
PRAI US 2000-244764P 20001031; US 2000-222056P 20000731; US 2001-920607 20010731
AB WO 200210750 A UPAB: 20020926
NOVELTY - Methods for detecting one or more non-nucleic acid analyte (NAA) using fusion polypeptides with specificity for the analyte, where the polypeptide comprises a first inactive functional domain, an analyte binding domain and a second inactive functional domain, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a method (M1) for detecting one or more NAA, comprising:

(a) providing at least one fusion polypeptide (P1) with specificity for a NAA, where P1 comprises a first inactive functional domain, an analyte binding domain, and a second inactive functional domain, where binding of the NAA results in a conformational change which brings the first inactive functional domain and the second inactive functional domain into proximity, therefore converting the first and second inactive functional domains into an optically detectable functional domain;

(b) contacting P1 with a sample comprising the NAA; and

(c) detecting the conformational change induced by binding of the NAA, where the NAA is selected from a small organic molecule, a peptide, a polypeptide and a dissolved gas;

(2) another method (M2) for detecting one or more NAA, comprising:

(a) step (a) of M1, where the first and second inactive functional domains are converted into a catalytic functional domain;

(b) providing a substrate for the catalytic functional domain;

(c) contacting the fusion polypeptide with a sample comprising the analyte; and

(d) detecting the conversion of the substrate to a product;

(3) another method (M3) for detecting one or more NAA, comprising:

(a) providing at least one polypeptide with specificity for a NAA, where the polypeptide comprises an analyte binding domain and a catalytic domain, where binding of the analyte results in an allosteric conformational change which activates the catalytic domain resulting in conversion of a substrate to a detectable product; and

(b) providing a substrate for the catalytic domain;

(c) contacting the polypeptide with a sample comprising the analyte; and

(d) detecting the product produced by activity of the catalytic domain on the substrate;

(4) a method (M4) for detecting an analyte, comprising providing at least one biopolymer which undergoes a conformational change upon binding to an analyte, contacting a sample comprising the analyte to the biopolymer; and detecting the conformation change induced by binding of the analyte, where the analyte is not an ion;

(5) a method (M5) for identifying a physiologic state, comprising providing at least one biopolymer which biopolymer undergoes a conformational change upon binding to a marker associated with a physiologic state, contacting the biopolymer with a biological sample comprising the marker, and detecting the conformation change induced by binding of the marker, thereby identifying the physiologic state associated with the marker;

(6) a biosensor comprising:

(a) a support; and

(b) at least one polypeptide with specificity for a NAA, where the polypeptide comprises an analyte binding domain and a catalytic domain, where binding of the analyte results in an allosteric conformational change which activates the catalytic domain resulting in conversion of a substrate to a detectable product, where the polypeptide is immobilized on the support; or

(c) at least one fusion polypeptide with specificity for a NAA, where the polypeptide comprises a first inactive functional domain, and analyte binding domain, and a second inactive functional domain, where binding of the analyte brings the first inactive functional domain and the second inactive functional domain into proximity, thereby converting the first and second inactive functional domains into a functional catalytic or optically detectable domain where the fusion polypeptide is immobilized on the support; or

(d) a polypeptides immobilized on the solid support, where the polypeptides having different analyte **binding** specificities, and a **detection** system;

(7) a method (M6) of sensing one or more test stimulus, comprising:

(a) providing a library of biopolymers comprising nucleic acid variants or expression products of the nucleic acid variants;

(b) arraying the library in a spatial or logical format to provide a physical or logical array;

(c) contacting one or more calibrating stimulus to the array, where one or more members of the array produce one or more detectable signals in response to contact by the one or more calibrating stimulus, thereby producing a calibrating array pattern which identifies contact of the array by the one or more calibrating stimulus;

(d) contacting at least one test stimulus to the array, thereby producing a test stimulus array pattern; and

(e) comparing the test stimulus array pattern to the calibrating array pattern, thereby identifying the test stimulus;

(8) a method (M7) of using a re-usable array of biopolymers, comprising:

(a) providing a physical or logical array of biopolymers comprising nucleic acid variants or expression products of the nucleic acid variants;

(b) contacting the physical or logical array with one or more first stimulus;

(c) observing a first resulting response of the array, or collecting a first product resulting from contact between the array and the first stimulus;

(d) reusing the array by contacting the array a second time with the first stimulus, or with a second stimulus, and observing a second resulting response of the array, or collecting a second product resulting from contact between the array and the first or second stimulus, and, optionally, comparing the first resulting response of the array to the second resulting response of the array;

(9) biopolymer array produced by M6 or M7; and

(10) a computer comprising a data set corresponding to the labeling biopolymer sensor array pattern or test biopolymer sensor array pattern of M6 or M7.

USE - The methods and biosensors are useful for detecting a wide

range of biological, chemical and biochemical stimuli, e.g. polypeptides, hormones, metabolite and small molecules. They are useful in medical, environmental and industrial diagnostic procedures, for e.g. the array can be used for detection of protein biomarkers associated with disease or other physiological condition.
Dwg.0/7

TECH UPTX: 20020424
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In M1, the first and second inactive functional domains are derived from a green fluorescent protein or a green fluorescent protein homologue.
M1 comprises **detecting** an electrochemical signal produced by binding of the **analyte** or **detecting** an optical signal produced by binding of the **analyte**.
The optical signal is **detected** by one or more of: ultraviolet spectrophotometry, visible light spectrophotometry, surface plasmon resonance; calorimetry, fluorescence polarization; fluorescence quenching; colorimetric quenching; fluorescence wavelength shift; fluorescence resonance energy transfer (FRET); enzyme linked immunosorbent **assay** (ELISA) or liquid crystal displays (LCD). The optical signal is produced by displacement of a tethered substrate upon binding of the **analyte**. The tethered substrate is an **analyte analogue**.
In M2, the conversion of the substrate to a product is **detected** by **detecting** an electrochemical signal or an optical signal which is **detected** as described above.
M1, M2, M3, M4 and M5 comprise providing a physical or logical array comprising polypeptides which have different **analyte** binding specificities. In M1, M2, M4 and M5, the polypeptides provide a common signal. The NAA comprises a small molecule, a hormone or a metabolite. The sample is a biological sample (blood, plasma, urine, sweat, cerebrospinal fluid and tears) or an environmental sample.
In M3, the conversion of the substrate to product produces an electrochemical signal or an optical signal which is **detected** as described above. In M3, the conversion of substrate to product by the **analyte**-bound polypeptides is **detected** by **detecting** a common signal. The sample is a biological sample, an environmental sample, or an industrial sample. The sample further comprises an agonist or an antagonist. The **analyte** comprises a small molecule, a hormone, a metabolite, an ion, an antigen or a ligand.
In M4, the biopolymer comprises a polypeptide which comprises an antibody or a receptor. The conformation change results in generation of an optical signal which is **detected** as described above. The optical signal is produced by displacement of a tethered substrate upon binding of the **analyte**. The tethered substrate is an **analyte analogue**.
In M5, the biopolymer comprises a polypeptide which comprises an enzyme, an antibody, a receptor or a fusion protein. Preferably the polypeptide is P1, where binding of the **analyte** results in a conformational change which brings the first inactive functional domain and the second inactive functional domain into proximity, thereby converting the first and second inactive functional domains into a functional catalytic or fluorescent domain. The conformation change results in generation of an optical signal which is **detected** as described above. The optical signal is produced by displacement of a tethered substrate upon binding of the **analyte**. The tethered substrate is an **analyte analogue**.
In M6 and M7, the biopolymer library comprises or is encoded by recursively recombined nucleic acids. The biopolymer library comprises or is encoded by artificially mutated or artificially shuffled nucleic acids. Alternatively, the biopolymer library comprises or is encoded by species

variants of one or more nucleic acids. Alternatively, the biopolymer library comprises or is encoded by nucleic acids produced by recursive recombination of species variants of one or more nucleic acids. The biopolymer library comprises photoactivatable members. The method comprises masking a portion of the array and exposing the resulting masked array to light. The array comprises one or more of a conductive member, a capacitive member, an optically responsive member, an electrically responsive member, and an electrically or logically gated or gateable member. Alternatively, the array comprises one or more of: a bio-laser, a polychromic display, a molecular poster, a bar code, a protein TV, a molecular camera, a UV (ultra-violet) molecular camera, an IR (infra-red) molecular camera, or a flat screen display. The array members comprise one or more proteins. The proteins comprise electrically conductive proteins. The proteins are purified. The proteins comprise one or more purification tags such as His tags, and FLAG tags.

Arraying the biopolymer library comprises:

(a) arranging the members of the library in a logically accessible format;

(b) arranging the members of the library in a physically grided format;

(c) plating the members of the library in microtiter trays; or

(d) arranging the members of the library for parallel examination.

Arraying the biopolymer library or expression product library comprises recording the position of members of the library in one or more database, or arranging the members of the library for sequential examination.

The first, second, test or calibrating stimulus are simultaneously, sequentially or alone contacted to biopolymer library members. Contact of the of first, second, test or calibrating stimulus produces a signature for a sample type. The signature is representative of one or more phenomenon selected from a metabolic state of a cell, an operon induction in or by a cell, an induction of cell growth, a proliferation in or caused by a cell, a cancer of a cell or tissue, or organism, apoptosis, cell death, cell cycle, cell or tissue differentiation, tumorigenesis, disease state, drug resistance, drug efficacy, antibiotic spectrum, drug toxicity, gas level, SOx, NOx Alzheimer's disease, infection, presence of viruses, viral infection, bacterial infection, HIV infection, AIDS, serum cholesterol, CHDL (undefined) level, LDL (low density lipoprotein), serum triglyceride level, blood glucose level, ion or gas production or internalization, cytokine receptor expression, antibody-antigen interactions, pregnancy, fertility, fecundity, presence or absence of narcotics or other controlled substances, heart attack, presence or absence of steroids, body temperature, presence of sound waves, taste, scent, food composition, beverage composition, and an environmentally monitored condition.

The first, second, test or calibrating stimulus are contacted to library members in a microtiter plate or fixed on a solid substrate. Alternatively, the first, second, test or calibrating stimulus are contacted to library members, or their expression products, fixed on a solid substrate, where the solid substrate comprises a Nickel-NTA coated surface, a silane-treated surface, a pegylated surface, or a treated surface. The biopolymer library members or expression products thereof are fixed to an organizational matrix in spatially addressable locations. Alternatively, the first, second, test or calibrating stimulus are contacted to biopolymer library members, where member types are fixed on the surface of one or more beads. One or more beads comprise more than one **detectable** feature. More than one **detectable** feature includes a first feature which identifies binding by the first, second, test or calibrating stimulus and a second feature which identifies either the type of bead or the type of library member or expression product thereof which is bound to the bead. The first stimulus, the second stimulus, the calibrating stimulus or the test stimulus, is selected from light, radiation, an atom, an ion, and a molecule.

The first, second, test or calibrating stimulus comprises, hybridizes to, binds, acts upon or is acted upon by one or more of: radiation, a polymer, a chemical group, a biopolymer, a nucleic acid, an RNA, a DNA, a protein, a ligand, an enzyme, a chemo-specific enzyme, a regio-specific enzyme, a stereo-specific enzyme, a **nuclease**, a restriction enzyme, an restriction enzyme which recognizes a triplet repeat, a restriction enzyme that recognizes DNA superstructure, a restriction enzyme with an 8 base recognition sequence, an enzyme substrate, a regio-specific enzyme substrate, a stereo-specific enzyme substrate, a ligase, a thermostable ligase, a polymerase, a thermostable polymerase, a co-factor, a lipase, a protease, a glycosidase, a toxin, a contaminant, a metal, a heavy metal, an immunogen, an antibody, a disease marker, a cell, a tumor cell, a tissue-type, cerebrospinal fluid, a cytokine, a receptor, a chemical agent, a biological agent, a fragrance, a pheromone, a hormone, an olfactory protein, a metabolite, a molecular camera protein, a rod protein, a cone protein, a light-sensitive protein, a lipid, a pegylated material, an adhesion amplifier, a drug, a potential drug, a lead compound, a protein allele, an oxidase, a reductase, or a catalyst.
The first, second, test or calibrating stimulus are contacted to the members of the library by incubating a solution comprising the test molecule or the calibrating molecule with the library members. The solution is a fluid, a polymer solution or a gel.
Comparison of the test array pattern and the calibrating array pattern, or of the first resulting response of the array and the second resulting response of the array, is performed by a computer. The first, second, test or calibrating stimuli are contacted to the array to produce resulting array patterns. The methods further comprise recording the resulting array patterns in one or more databases, and assigning a bar code to each resulting array pattern.
The test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array, comprises variations in the presence or absence of signal at different locations on or in the array. The test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array comprises variations in the level of signal at different locations on the array. The test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array comprises variations in the presence and intensity of signal at different locations on the array. An intensity of the test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array comprises is measured to quantify the first, second, test or calibrating stimulus.
The test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array comprises one or more fluorophore emission, photon emission, chemiluminescent emission, coupled luminescent/fluorescent emission or quenching, or **detection** of one or more fluorophore emission. The test array pattern, the calibrating array pattern, the first resulting response of the array, or the second resulting response of the array comprises an electrochemically **detectable** signal, an amperometrically **detectable** signal, a potentiometrically **detectable** signal, a signal **detectable** as a change in pH, a signal based on specific ion levels, a signal based on changes in conductivity, a pizoelectric signal, a change in resonance frequency, a signal **detectable** as surface accoustic waves, or a signal **detectable** by quartz crystal microbalances. The test array pattern, the calibrating array pattern, the first resulting response of the array or the second resulting response of the array comprises multiple wavelengths of light.

The test array pattern, the calibrating array pattern, the first resulting response of the array or the second resulting response of the array is generated by **detection** of one or more of: light, H2O2, glucose oxidase, NADP, NADPH+, **NAD**(P)H reductase, a change in reduction potential, a change in protein conformation, a change in intrinsic fluorescence, fluorescence, luminescence, FRET, absorption, surface plasmon resonance, antigen binding, antibody binding, enzyme activity, opening of an ion channel, or label binding. At least one member of the biopolymer library, or an expression product thereof, is selected, prior to the arraying step, for one or more of: enhanced stability, orientation of protein binding, improved production, cost of manufacture, optimal activity of expressed members which comprise a tag, overexpression mutations, optimized protein folding, permanent enzyme secretion, improved operators, improved ribosome binding sites, avidity, selectivity, production of a **detectable** side product, and **detection** limit.

The test array pattern, the calibrating array pattern, the first resulting response of the array or the second resulting response of the array are **detected** by one or more of: a microscope, a CCD, a phototube, a photodiode, an LCD (liquid crystal display), a scintillation counter, film, or visual inspection. The test array pattern, the calibrating array pattern, the first resulting response of the array or the second resulting response of the array are digitized and stored in one or more database in one or more computer.

M6 and M7 further comprise contacting at least one additional stimulus to the array, and comparing a resulting additional test stimulus array pattern to the calibrating array pattern, thereby identifying the at least one additional stimulus, or observing an additional resulting response of the array, or collecting an additional product resulting from contact between the array and the additional or a previous stimulus, and optionally comparing the additional resulting response to any one or more previous responses of the array.

The method **comprises** contacting the array with 2, preferably 10, or more additional stimuli.

Preferred Biosensor: The biosensor further comprising a conductive element or an optically detectable element. The polypeptides are immobilized with an immobilization matrix selected from carbon paste and a non-biological polymeric matrix. The biosensor further comprises a display.

Preferred Biopolymer Array: The biopolymer array is stable for at least one year under pre-selected storage conditions.

L30 ANSWER 3 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-194575 [25] WPIDS
CR 2000-182334 [13]
DNC C2002-060071
TI New 2'-modified oligonucleotides having alternating internucleoside linkages, useful for inhibiting the production or activity of a protein and treating e.g. psoriasis.
DC A96 B04
IN MANOHARAN, M
PA (ISIS-N) ISIS PHARM INC
CYC 1
PI US 6326358 B1 20011204 (200225)* 28p
ADT US 6326358 B1 CIP of US 1998-115025 19980714, US 1999-349007 19990707
PRAI US 1999-349007 19990707; US 1998-115025 19980714
AB US 6326358 B UPAB: 20020418
NOVELTY - Oligonucleotides containing at least 1 region of 2'-modified **nucleosides** connected by alternating phosphodiester and phosphorothioate linkages are new.

DETAILED DESCRIPTION - Compounds comprising covalently bound

2'-modified **nucleosides** of formula (I) are new:

1 of X1 or X2 is O and the other is S;

B = a nucleobase;

R1 = OH, 1-20C alkyl, 3-20C alkenyl, 2 20C alkynyl, halo, thiol, keto, carboxyl, NO2, nitroso, CN, CF3, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, NH2, N phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, Z-R22-(R23)v, -(O)y1-(-(CH2)y2-O-N(Q1)-)y3-(CH2)y2 O-E, -(-Z0-(CH2)q1-)q2-(O)q3-E or a group of formula (A):

Z = O, S, NH or N-R22-(R23)v;

R22 = 1-20C alkyl, 2-20C alkenyl or 2-20C alkynyl;

R23 = H, NH2, halo, OH, thiol, keto, carboxyl, NO2, nitroso, CN, CF3, trifluoromethoxy, O alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O aralkyl, S-aralkyl, NH-aralkyl, NH2, phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol or polyether;

v, y2, q1 = 0-10;

y1, q3, m = 0 or 1;

y3, q2 = 110;

q4 = 0-2;

E = 1-10C alkyl, N(Q1)(Q2) or N=C(Q1)(Q2);

Q1, Q2 = H, 1-10C alkyl, optionally substituted alkyl, dialkylaminoalkyl, N-protecting group, optionally tethered conjugate group, or a linker to a solid support; or

Q1+Q2 = joined in a N-protecting group or a ring structure optionally including at least 1 additional heteroatom (N or O);

Z0 = O, S or NH;

Z4 = OM1, SM1 or N(M1)2;

M1 = H, 1-8C alkyl, 1-8C haloalkyl, C(=NH)N(H)M2, C(=O)N(H)M2 or OC(=O)N(H)M2;

M2 = H or 1-8C alkyl;

Z1, Z2, Z3 = ring system having 4-7C, or 3-6C and 1 or 2 heteroatoms (O, N or S), where the ring is optionally unsaturated aliphatic, aromatic, or optionally unsaturated heterocyclic;

Z5 = 1-10C alkyl, 1-10C haloalkyl, 2-10C alkenyl, 2-10C alkynyl, 6-14C aryl, N(Q1)(Q2), OQ1, halo, SQ1 or CN;

n = 2-50; and

m = 0 or 1.

INDEPENDENT CLAIMS are included for the following:

(1) oligonucleotides of formula (II); and

(2) oligonucleotides of formula (5')-W1-W2-W3-(3') (III).

W1 = a group of formula (IV): 1 of X'1 or X'2 is O and the other is S;

W3 = a group of formula (V):

W2 = covalently bound **nucleosides** linked by phosphodiester or phosphorothioate linkages.

X'1 = S;

X'2 = O;

R2 = H, a hydroxyl protecting group, or an oligonucleotide;

R3 = OH, an oligonucleotide, or a linker connected to a solid support;

ACTIVITY - Antipsoriatic; antiinflammatory; dermatological; antipruritic; cytostatic; antibacterial; virucide; fungicide.

MECHANISM OF ACTION - Protein binding modulators; DNA modulators; RNA modulators.

A test was carried out to determine inhibition of ICAM-1 expression in HUVEC cells. Oligomers tested included TCTGAGTAGCAGAGGAGCTC asterisk (backbone P=S/P=O, 2'-O-CH2CH2-O-CH3) (Ia), a P=O oligomer, a P=S oligomer, and controls (scrambled oligomers having the same base compositions as the parent sequence). The ICAM-1 expression data showed that the staggered oligomer (Ia) is more efficacious than both the P=O oligomer and P=S oligomer in HUVEC cells.

USE - For inhibiting the production or activity of a protein in an organism (claimed). The oligonucleotides can be used in diagnostics, therapeutics and as research reagents and kits; for treating e.g. psoriasis and inflammatory disorders of the skin (such as lichen planus, toxic epidermal necrolysis, erythema multiform), skin cancer, infectious disorders of the skin (bacterial, viral or fungal).

ADVANTAGE - The compounds are resistant to nuclease degradation, and have increased binding affinity relative to phosphorothioate oligomers. The staggered phosphorothioate/phosphodiester linkages will also modulate the protein binding to plasma proteins.

Dwg.0/3

TECH UPTX: 20020418

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preparation: The oligonucleotides are prepared by conventional synthetic methods.

Preferred Compounds:

R1 = -O-CH2-CH2-O-CH3;

n = 2-10;

R2 = H;

R3 = OH;

R2,R3 = preferably phosphodiester-linked oligonucleotide or phosphorothioate-linked oligonucleotide;

L30 ANSWER 4 OF 24 WPIDS (C) 2002 THOMSON DERWENT

AN 2002-097573 [13] WPIDS

DNC C2002-030374

TI Improving pharmacokinetics of drugs metabolized by cytochrome p450 enzyme by co-administering phosphorodiamidate morpholino oligonucleotide which is antisense to RNA encoding the enzyme.

DC B04 D16

IN IVERSEN, P L

PA (AVIB-N) AVI BIOPHARMA INC

CYC 96

PI WO 2001087286 A2 20011122 (200213)* EN 58p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001063197 A 20011126 (200222)

ADT WO 2001087286 A2 WO 2001-US15857 20010516; AU 2001063197 A AU 2001-63197 20010516

FDT AU 2001063197 A Based on WO 200187286

PRAI US 2000-737452 20001213; US 2000-574570 20000517

AB WO 200187286 A UPAB: 20020226

NOVELTY - Improving in a subject the pharmacokinetics of a drug, comprising co-administering with the drug a morpholino antisense oligomer by oral or transdermal route effective to reduce synthesis of a drug-metabolizing cytochrome p450 enzyme that reduces the effectiveness of the drug, by hybridizing to a target RNA molecule which encodes the enzyme, is new.

USE - The method is useful for improving the performance of drugs which are metabolized by cytochrome p450 enzyme.

ADVANTAGE - The oligomers reduce production of the drug-metabolizing enzymes, which extends drug half-life and effectiveness and/or decreases drug toxicity. The oligomers have very high **nuclease** resistance and good water solubility. Since they are uncharged they are more effective in penetrating cell membranes. Cell viability of primary human hepatocytes and caco-2/h3A4 cells (human colon carcinoma cell line caco-2 transfected with CYP3A4 cDNA on an extrachromosomal vector p220CMV3A4) was assessed following co-treatment with the antisense phosphorodiamidate morpholino oligonucleotide (PMO) having the sequence CTGGGATGAGAGCCATCACT, or control PMO in combination with three cytotoxic drugs, paclitaxel metabolized to less cytotoxic metabolites by CYP3A4, cyclophosphamide that required metabolic activation by CYP3A4 to become cytotoxic, and cisplatin not metabolized by CYP3A4. Cells were treated with PMO 24 hours prior to addition of cytotoxic drugs. Cell viability was **determined** by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl **tetrazolium** bromide (MTT) **assay** after an additional 24 hours incubation with 5 micro M paclitaxel, 600 micro M cyclophosphamide or 7 micro M cisplatin. Addition of the antisense PMO in combination with paclitaxel reduced cell viability in both model systems. Co-treatment of cells with the antisense PMO and cyclophosphamide significantly increased the cell viability in both model systems compared to treatment with cyclophosphamide alone. Co-treatment of cells with cisplatin and the antisense PMO did not significantly alter cell viability from the moderately cytotoxic dose of cisplatin.

Dwg.0/7

TECH UPTX: 20020226

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The morpholino oligomer has intersubunit linkages chosen from formulae (A)-(D).

The linkages are phosphorodiamidate linkages as shown formula (B), where:

X = NH2, NHR, NRR' or OR;

Y = O, NH or NR'; and

Z' = O; and

NRR' = nitrogen heterocycle with 5-7 ring atoms chosen from nitrogen, carbon, oxygen or sulfur and having as many carbon ring atoms as non-carbon ring atoms.

R and R' are groups which do not interfere with target binding such as alkyl, polyalkyleneoxy, or their combination, which may be substituted with one or more groups such as hydroxy, alkoxy, amino, alkylamino, thiol, alkanethiol, halogen, oxo, carboxylic acid, carboxylic ester and inorganic ester, independent of substitution and is from 1-6 atoms in length.

The antisense oligomer is 15 nucleotides in length and hybridizes to a region of the target RNA with a Tm greater than 37 degrees C, or to a region of the target RNA which includes the AUG translation start site. The target RNA molecule is pre-mRNA, and the antisense oligomer hybridizes to a region of the pre-mRNA which includes an intron-exon boundary or an exon-intron boundary. The drug induces the drug-metabolizing cytochrome p450 enzyme, or is administered to a subject who has been exposed to a xenobiotic agent which induces such an enzyme. The drug induces the cytochrome p450 enzyme such as CYP1A1, CYP1A2, CYP2A6, CYP2B1, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A2, CYP3A4 and CYP6A1. The enzyme is preferably CYP2E1 and the drug is acetaminophen, the enzyme is CYP2B or CYP3A subfamily and the drug is phenobarbital or hexobarbital. The enzyme is CYP3A4 and the drug is an antibiotic such as clarithromycin, erythromycin, rifampicin, rifampin, rifabutin and rapamycin, or paclitaxel, or a protease inhibitor or non-**nucleoside** reverse transcriptase (RT) inhibitor and the xenobiotic agent is a CYP3A4-inducing non-**nucleoside** RT inhibitor, or the enzyme is CYP3A4 or CYP1A2 and the drug contains an estrogen or estradiol.

L30 ANSWER 5 OF 24 WPIDS (C) 2002 THOMSON DERWENT

AN 2002-010797 [01] WPIDS
DNC C2002-002654
TI Amplifying a target nucleic acid, useful in e.g. research and forensic science, by combining a target nucleic acid with reversibly modified nucleic acid primers and **nucleoside** triphosphates to inhibit formation of undesired products.
DC B04 D16
IN BONNER, A G
PA (BIOL-N) BIOLINK PARTNERS INC
CYC 95
PI WO 2001075139 A1 20011011 (200201)* EN 45p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001053129 A 20011015 (200209)
ADT WO 2001075139 A1 WO 2001-US10901 20010403; AU 2001053129 A AU 2001-53129 20010403
FDT AU 2001053129 A Based on WO 200175139
PRAI US 2000-194288P 20000403
AB WO 200175139 A UPAB: 20020105
NOVELTY - Amplifying a target nucleic acid, comprising combining a target nucleic acid with one or more nucleic acid primers and **nucleoside** triphosphates which have been reversibly modified to inhibit the formation of undesired amplification products, under conditions allowing amplification to occur, is new.

DETAILED DESCRIPTION - Amplifying a target nucleic acid comprises combining a target nucleic acid with one or more nucleic acid primers capable of binding to the target nucleic acid, a nucleic acid polymerase, and several **nucleoside** triphosphates, where the target nucleic acid, primers and **nucleoside** triphosphates have been reversibly modified to inhibit the formation of undesired amplification products, thus forming a resultant mixture resulting in the selective amplification of the target nucleic acid.

INDEPENDENT CLAIMS are also included for the following:

(1) an amplified nucleic acid produced by the novel method;

(2) a **kit** for conducting polymerase chain reaction (PCR) comprising a reagent for reversibly chemically modifying a nucleic acid or nucleobase so that when the nucleic acid is used in the reaction, the formation of undesired amplification products is inhibited, and instructions for use; and

(3) a compound which can amplify a target nucleic acid and reduce undesired amplification products, comprising a reaction mixture of a removable protecting group and **guanosine** 5'-triphosphate.

USE - The amplification method is also advantageously used to amplify virtually any target nucleic acid such as a nucleic acid fragment, gene fragment, cDNA or chromosomal fragment. The methods and compositions permit the **detection** and amplification of small amounts of nucleic acid, and as such are applicable to diagnostic applications, research and forensic science. The methods and compositions are also useful to **detect** or characterize nucleic acid sequences associated with infectious diseases, genetic and non-genetic disorders, or cellular disorders such as cancer; and to **detect** viral nucleic acid molecule within a nucleic acid sample derived from human cell sample, cancerous cells by **detecting** specific chromosomal rearrangements or changes in gene expression, and the sex or species of origin of even minute biological samples. These are also used in research applications in which genetic **analyses** must be performed on limited amounts of

nucleic acid sample or in the presence of background DNA. The reversibly modified nucleic acids are used to prevent or disrupt hybridization during routine sample preparation, and provide **nuclease** resistance to nucleic acids which may be applications in therapeutics. Hypersensitive protecting groups may provide improved approaches to drug delivery and gene therapy.

ADVANTAGE - The method does not require manipulation of the reaction mixture following initial preparation, may be used in existing automated PCR amplification systems and with in situ amplification methods where addition of reagents after the initial denaturation step is inconvenient or impractical.

Dwg.0/11

TECH UPTX: 20020105

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The reversibly modified target nucleic acid or primers comprise at least one nucleobase that has been reversibly modified chemically, where the primers are reversibly modified to inhibit the formation of undesired amplification products. The amplification which is by PCR, preferably hot-start PCR, results in a reduced amount of non-specific nucleic acid amplification products. The reversibly modified nucleobase comprises a removable protecting group selected from glyoxal dihydrate, glyoxal hydrogen sulfite, 2,3-dihydroxy-1,4-dioxane, pyruvaldehyde (methylglyoxal), 2,3-butanedione (dimethylglyoxal), 2,3-pentadione (ethylmethylglyoxal), phenylglyoxal, and di-3-pyridylglyoxal, preferably glyoxal. Alternatively, the removable protecting group is selected from 3,4,5,6,-tetrahydrophthalic anhydride, 3-ethoxy-2-ketobutyraldehyde (kethoxal), ninhydrin, hydroxyacetone, diethyl oxalate, diethyl me oxalate, 1,2-naphthoquinone-4-sulfonic acid, pyruvaldehyde, gamma-carboxyacylamides, amidines and carbamates. The amide is a trifluoroacetyl or trichloroacetyl. The gamma-carboxyacylamide is acontinoyl, maleyl, citriconyl, phenoxyacetyl or acetoacetyl. The amidine is imidoamide, and the carbamate is ethoxycarbonyl. The method also includes heating the resultant mixture for a time sufficient to remove the protecting group. The resultant reaction mixture is subjected to at least one thermal cycle. The polymerase is an E. coli DNA polymerase I, TAQ polymerase, Kloenow fragment of E. coli DNA polymerase I, reverse transcriptase, and thermostable DNA polymerase. The polymerase is a thermostable DNA polymerase.

Preferred **Kit**: The **kit** further comprises a nucleic acid primer or a nucleic acid polymerase, and at least one other component for conducting polymerase amplification reaction.

L30 ANSWER 6 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-541322 [60] WPIDS
DNC C2001-161542
TI Novel polymerase protein useful for in vitro synthesis, amplification and stabilization of nucleic acids, especially RNA, and for determination of nucleotide base sequence of linear nucleic acid molecule.
DC A96 B04 C06 D16
IN BAMFORD, D; MAKEYEV, E
PA (BAMF-I) BAMFORD D; (MAKE-I) MAKEYEV E
CYC 95
PI WO 2001046396 A1 20010628 (200160)* EN 63p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001025181 A 20010703 (200164)

EP 1242586 A1 20020925 (200271) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001046396 A1 WO 2000-FI1135 20001221; AU 2001025181 A AU 2001-25181 20001221; EP 1242586 A1 EP 2000-988824 20001221, WO 2000-FI1135 20001221
FDT AU 2001025181 A Based on WO 200146396; EP 1242586 A1 Based on WO 200146396
PRAI FI 1999-2751 19991221
AB WO 200146396 A UPAB: 20011018
NOVELTY - An isolated polymerase protein (I), which has an unspecific capability of RNA synthesis in vitro when contacted with nucleic acid substrates under sufficient conditions, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a vector (II) comprising a nucleic acid sequence encoding (I);
(2) a host cell (III) comprising (II) or a nucleic acid sequence encoding (I);
(3) producing RNA in vitro, comprising:
(a) providing single stranded RNA (ssRNA) or double stranded RNA (dsRNA) or ssDNA or dsDNA substrate;
(b) contacting the ssRNA, dsRNA, ssDNA, or dsDNA substrate with (I); and
(c) recovering the newly produced RNA species from the reaction mixture;
(4) amplifying or producing RNA in vitro comprising:
(a) providing RNA substrate;
(b) contacting the RNA substrate with (I) under conditions sufficient for both RNA-replication and RNA-transcription; and
(c) recovering a mixture of the newly produced amplified RNA from the reaction mixture;
(5) stabilizing nucleic acids comprising:
(a) providing single-stranded nucleic acid substrate;
(b) contacting the single-stranded nucleic acid substrate with (I) under conditions sufficient for RNA synthesis in order to convert at least part of the single-stranded nucleic acid substrate to the double-stranded nucleic acid form;
(c) recovering total nucleic acids from the reaction mixture; and optionally
(d) contacting the total nucleic acids with a preparation containing nuclease or nucleases selectively degrading single-stranded nucleic acids by not double-stranded nucleic acids; and
(e) recovering the double-stranded nucleic acids showing increased stability to the degradation by nucleases;
(6) producing RNA in vitro comprising:
(a) providing RNA or DNA substrate;
(b) contacting the RNA or DNA substrate with (I) under conditions sufficient for RNA synthesis in a mixture comprising nucleic acid substrate, (I), **nucleoside** triphosphates, and optionally buffer, ammonium acetate, DTT, PEG, Mg2+-ions, Mn2+-ions and/or bovine serum albumin (BSA); and
(c) incubating the reaction mixture at temperature sufficient for RNA synthesis; and
(d) recovering the newly produced nucleic acid species from the reaction mixture;
(7) determining the nucleotide base sequence of a linear nucleic acid molecule comprising:
(a) providing linear nucleic acid molecule;
(b) incubating the nucleic acid molecule under conditions sufficient for RNA synthesis in a mixture comprising:
(i) (I);
(ii) four **nucleoside**-triphosphates or functional analogs of

it; and

(iii) at least one of four RNA synthesis terminating agents which terminate RNA synthesis at a specific nucleotide base, where each of the agent terminates RNA synthesis at a different nucleotide base; and

(c) separating the terminated RNA products of the incubating reaction according to their sized, where at least a part of the nucleotide base sequence of the nucleic acid molecule can be determined;

(8) producing, isolating and purifying (I); and

(9) a kit for producing RNA in vitro, comprising (I) and optionally, additives necessary for a detectable level of RNA synthesis.

USE - Novel polymerase proteins can be used in the synthesis of RNA in the presence of different RNA and DNA templates. Methods of the invention may be used for stabilizing and sequencing nucleic acids. The methods are useful for detecting pathogenic parasites and differences in gene expression levels associated with diseases.

ADVANTAGE - The polymerase is highly processive, has very high RNA-polymerization rate, and does not require primer for the initiation of RNA synthesis, although it is also able to initiate RNA synthesis in the presence of a primer. The polymerase has low template specificity being able to catalyze RNA synthesis in the presence of ssRNA, dsRNA, ssDNA and dsDNA substrates, preferably in the linear form.

Dwg.0/11

TECH UPTX: 20011018

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: (I) is produced by culturing (III) to express the protein, recovering the protein from the host or from the culture medium by disrupting the host cells in a buffer to obtain a cell lysate, clarifying the lysate by centrifugation, purifying the protein using at least one step, more preferably two steps of affinity chromatography, further purifying the protein using at least one step of ion exchange chromatography to obtain a fraction that is essentially free of **nuclease** and protease activities, and optionally, **assaying** the RNA-synthesizing activity of protein (claimed).

Preferred Protein: (I) originates from double-stranded (dsRNA)-viruses e.g., Cystoviridae, Reoviridae, Birnaviridae or Totiviridae-viruses, preferably from phi6-related bacteriophages from the family of Cystoviridae, such as from phi6 to phi14. (I) is P2 protein of bacteriophage phi6 of Pseudomonas syringae, or its altered or genetically modified. (I) is encoded by a nucleic acid sequence having at least a partial sequence (S1) of 1998 nucleotides fully defined in the specification, a nucleic acid sequence encoding a polypeptide having at least a partial sequence (S2) of 665 amino acids fully defined in the specification, a nucleic acid sequence, which differs from the above said sequences due to degeneracy of the genetic code, a nucleic acid sequence hybridizing to the above nucleic acid sequences, or a nucleic acid sequence encoding an amino acid sequence which shows at least 20%, preferably at least 50%, identity to a sequence contained in a sequence encoding S2. DNA dependent RNA polymerase is derived from a T7, T3 or SP6 bacteriophage. The newly produced nucleic acid species using (I) comprises duplexes consisting of template DNA and RNA replica. The single-stranded or double-stranded nucleic acid substrate is linear. The mixture for RNA synthesis contains at least one **nucleoside** triphosphate labeled with a radioactive isotope or is chemically modified. RNA synthesis is initiated from the 3' end of a primer complementary to the nucleic acid substrate. The primer is a single-stranded RNA or DNA.

Preferred **Kit**: The **kit** comprises **nucleoside** triphosphates in concentrations sufficient for RNA synthesis. At least one **nucleoside** triphosphate is labeled with a radioactive isotope or is chemically modified. The **kit** additionally contains a standard nucleic acid preparation (or preparations) with characterized capacity to

serve as a template (templates) for RNA synthesis. The **kit** is specifically used for sequencing nucleic acid molecule, and optionally, comprising at least one RNA synthesis terminating agent which terminate RNA synthesis at a specific nucleotide base. RNA synthesis terminating agent is a 3'-deoxynucleotide triphosphate or its functional derivative. At least one of the **nucleoside**-triphosphates or its **analogs** is modified to contain **detectable** label. At least one of RNA synthesis terminating agents is modified to contain **detectable** label.

L30 ANSWER 7 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-536643 [59] WPIDS
DNC C2001-159819
TI Detecting abnormal base-pairing, mutation in nucleic acid, or polymorphism in gene locus, comprises contacting nucleic acid with abnormal base-pairing and mutant nucleic acid repair enzyme, and **detecting** their **binding**.
DC B04 D16
IN YUAN, C
PA (GEAT) GEN ATOMICS
CYC 93
PI WO 2001062968 A2 20010830 (200159)* EN 294p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001027679 A 20010903 (200202)
ADT WO 2001062968 A2 WO 2001-US452 20010105; AU 2001027679 A AU 2001-27679 20010105
FDT AU 2001027679 A Based on WO 200162968
PRAI US 2000-514016 20000225
AB WO 200162968 A UPAB: 20011012
NOVELTY - Detecting (M1) abnormal base-pairing in a nucleic acid duplex, mutation in a nucleic acid or polymorphism in a gene locus, comprising contacting a nucleic acid duplex having an abnormal base-pairing with a mutant nucleic acid repair enzyme (I) or its complex, and **detecting** the **binding** between the nucleic acid duplex and (I), such that the presence of abnormal base-pairing, mutation or polymorphism is detected, is new.

DETAILED DESCRIPTION - M1 comprises:

(a) detecting abnormal base-pairing in a nucleic acid duplex, by contacting a nucleic acid duplex having or suspected of having a abnormal base-pairing with (I), where (I) has binding affinity for the abnormal base-pairing in the duplex but has attenuated catalytic activity compared to the wild-type enzyme, and **detecting** the **binding** between the nucleic acid duplex and (I), where the presence or quantity of the abnormal base-pairing in the duplex is assessed;

(b) detecting a mutation in a nucleic acid, by hybridizing a strand of a nucleic acid having or suspected of having a mutation with a complementary strand of a nucleic acid fragment having a wild type sequence, such that the mutation results in an abnormal base-pairing in the formed nucleic acid duplex, contacting the nucleic acid duplex with (I), and **detecting binding** between the nucleic acid duplex and (I), such that the presence or quantity of the mutation is assessed; or

(c) detecting polymorphism in a gene locus, by hybridizing a target strand of a nucleic acid comprising a locus to e tested with a complementary reference strand of a nucleic acid comprising a known allele

of the locus, such that the allelic identity between the target and the reference strands results in the formation of a nucleic acid duplex without an abnormal base-pairing and the allelic difference between the target and the reference strands results in the formation of a nucleic acid duplex with an abnormal base-pairing, contacting the nucleic acid duplex with (I), and **detecting binding** between the nucleic acid duplex and (I), such that the polymorphism in the locus is assessed.

INDEPENDENT CLAIMS are also included for the following:

(1) purifying or separating (M2) nucleic acid duplex containing one or more abnormal base-pairing from a population of nucleic acid duplexes, by contacting a population of nucleic acid duplexes having or suspected of having a nucleic acid duplex containing one or more abnormal base-pairing with (I), where the nucleic acid duplex containing one or more abnormal base-pairing binds to (I) to form a binding complex, and removing the nucleic acid duplexes that contain the binding complex from the population of nucleic acid duplexes;

(2) detecting and localizing (M3) an abnormal base-pairing in a nucleic acid duplex, by contacting a nucleic acid duplex having or suspected of having an abnormal base-pairing with (I) to form a binding complex, subjecting the nucleic acid duplex to hydrolysis with an exonuclease under conditions such that the binding complex blocks hydrolysis, and determining the location within the nucleic acid duplex protected from the hydrolysis, and thus detecting and localizing the abnormal base-pairing in the nucleic acid duplex;

(3) a combination (C1) for detecting abnormal base-pairing in a nucleic acid duplex, comprising (I), and a reagent for **detecting binding** between abnormal base-pairing in a nucleic acid duplex and (I);

(4) a **kit** comprising C1 and instructions for binding (I) to nucleic acid duplexes to detect a mutation in a nucleic acid duplex, to detect a polymorphism in a locus, to diagnose diseases or disorders, or for gene mapping or identification by detecting a number of polymorphisms or mutations;

(5) an isolated substantially pure (I) comprising a detectable label, and having attenuated catalytic activity compared to the wild-type but retaining binding affinity for a nucleic acid duplex containing an abnormal base-pairing;

(6) an article of manufacture, comprising a packaging material, (I), and a label indicating that the article is for use in detecting abnormal base-pairing in a nucleic acid duplex;

(7) a combination (C2) for detecting and localizing an abnormal base-pairing in a nucleic acid duplex, comprising (I) and an exonuclease; and

(8) a **kit** comprising C2 and instructions for performing an **assay** for detecting and localizing an abnormal base-pairing a nucleic acid duplex.

USE - The method is useful for prognosis or diagnosis of the presence or severity of the disease, disorder or infection by a pathological agent, associated with the mutation, including cancer, immune system disorder, metabolism disorder, muscle and bone disorder, nervous system disorder, signal disorder and transporter disease or disorder (claimed).

ADVANTAGE - The method is rapid and accurate, and is amenable to high throughput formats. The method requires neither specific probes nor gel electrophoresis. The method is amendable to automation for simultaneous detection of a large number of nucleic acid mutations.

Dwg.0/0

TECH UPTX: 20011012

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Mutant: The nucleic acid duplex is selected from DNA:DNA (preferred), DNA:RNA and an RNA:RNA

duplex. The abnormal base-pairing is selected from a base-pair mismatch e.g. single base-pair mismatch, a base insertion, base deletion and a pyrimidine dimer. (I) is selected from a mutant forms of mutH, mutL, mutM, mutS, mutY, uvrD, dam, **thymidine** DNA glycosylase (+TDG), mismatch-specific DNA glycosylase (MUG), AlkA, MLH1, MSH2, MSH3, MSH6, Exonuclease I, T4 endonuclease V, FEN1 (RAD27), DNA polymerase DELTA, DNA polymerase epsilon, RPA, PCNA, RFC (all undefined), Exonuclease V, DNA polymerase III holoenzyme, DNA helicase, RecJ exonuclease and their combinations. (I) comprises a fusion protein or conjugate of the mutant enzyme and an enzyme label.
Preferred Method: The nucleic acid duplex is formed by hybridizing a single strand of nucleic acid that contain a known sequence with a nucleic acid from a test sample, such that the binding of the mutant enzyme to any duplexes indicates the presence of a sequence difference in the nucleic acid from the sample from that of the nucleic acid containing the known sequence. The single strands of nucleic acid fragments with known sequences are immobilized on a solid support. The fragments are arranged in an array and the method is automated. Mutations are identified by hybridizing nucleic acid single strands to a number of different fragments comprising loci encompassing different mutations. The reference strands are hybridized, and immobilized on a solid support or in an array. The polymorphism to be **detected** is a variable nucleotide type polymorphism (VNTR) or a single nucleotide polymorphism (SNP) e.g. human genome SNP. The hybridization between the target strand of a nucleic acid comprising a locus to be tested and the complementary reference strand of a nucleic acid comprising a known allele of the locus is facilitated by a recombinase. The population of nucleic acid duplexes is produced by an enzymatic amplification. The exonuclease in M3 is selected from **nuclease** BAL-31, exonuclease III, Mung Bean exonuclease and Lambda exonuclease. (I) is labeled with biotin. The binding between the abnormal base-pairing and the biotin-labeled (I) is **detected** with a streptavidin labeled enzyme, selected from peroxidase, urease, alkaline phosphatase, luciferase and glutathione S-transferase. The nucleic acid duplex or (I) is immobilized on the surface of a support either directly or through a linker. The insoluble support is a silicon chip and the geometry of the support is selected from beads, pellets, disks, capillaries hollow fibers, needles, solid fibers, random shapes, thin films, membranes and chips. The nucleic acid duplex or (I) is immobilized in an array or a well format on the surface. The strand of a nucleic acid having or suspected of having a mutation, the complementary strand of a wild-type nucleic acid, or (I) is immobilized on the surface of a support. The target strand of a nucleic acid comprising a locus to be tested, the complementary reference strand of a nucleic acid comprising a known allele of the locus or (I) is immobilized on the surface of a support. The nucleic acid duplex having or suspected of having an abnormal base-pairing is isolated from a sample such as bodily fluid e.g. urine, blood, plasma, serum, saliva, semen, stool, sputum, cerebral spinal fluid, tears, mucus and amniotic fluid, or a biological tissue e.g. connective tissue, epithelium tissue, muscle tissue, nerve tissue, organs, tumors, lymph nodes, arteries and individual cell(s). The abnormal base-pairings, mutations and polymorphisms in a number of the nucleic acid duplexes are **detected** and localized simultaneously. The number of nucleic acids containing one or more abnormal base-pairing are removed simultaneously.

L30 ANSWER 8 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-388462 [41] WPIDS
CR 1992-080013 [10]; 1992-096815 [12]; 1992-415799 [50]; 1992-415800 [50]; 1994-026130 [03]; 1998-008042 [01]
DNC C2001-118466
TI Oligonucleotide **analog** for diagnostic, research and therapeutic

use is **nuclease** resistant.
DC B04 B05 D16
IN COOK, P D; SANGHVI, Y S
PA (ISIS-N) ISIS PHARM INC
CYC 1
PI US 6214551 B1 20010410 (200141)* 61p
ADT US 6214551 B1 CIP of US 1990-558663 19900727, CIP of US 1990-566836 19900813, CIP of US 1991-703619 19910521, CIP of WO 1992-US4294 19920521, CIP of US 1992-903160 19920624, Div ex US 1994-317289 19941003, CIP of US 1995-395168 19950227, US 1998-123572 19980727
FDT US 6214551 B1 CIP of US 5138045, CIP of US 5223618, CIP of US 5378825, CIP of US 5610289, CIP of US 5623070, Div ex US 5792844
PRAI US 1998-123572 19980727; US 1990-558663 19900727; US 1990-566836 19900813; US 1991-703619 19910521; WO 1992-US4294 19920521; US 1992-903160 19920624; US 1994-317289 19941003; US 1995-395168 19950227
AB US 6214551 B UPAB: 20010724
NOVELTY - A method for **assaying** a sequence-specific nucleic acid comprises contacting the test solution with the nucleotide analog (I).
DETAILED DESCRIPTION - A method for **assaying** a sequence-specific nucleic acid comprises contacting the test solution with the nucleotide analog of formula (I).
L1-L2-L3-L4 = CH2-NR1-NR2-CH2, CH2-CH2-NR1-NR2, or NR1-NR2-CH2-CH2;
R1,R2 = H; alkyl or substituted 1-10C-alkyl, optionally substituted 2-10C alkenyl; optionally substituted 2-10C alkynyl; optionally substituted 7-14C-aralkyl; alicyclic; heterocyclic; a reporter molecule;
B = a **nucleosidic** base;
Q = O, S, CH2, CHF or CF2;
n = greater than 0; and
X = H, OH, 1-10C - lower alkyl, substituted lower alkyl, alkaryl or aralkyl, F, Cl, Br, CN, CF3, OCF3, OCN, O-alkyl, S-alkyl, N-alkyl, O-alkenyl, S-alkenyl, N-alkenyl, SOCH2, SO2CH3ONO2, NO2, N3, H2, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino or substituted silyl.
USE - (I) is used in the diagnostic, research and therapeutics. It is capable of altering the activity of DNA and RNA activity.
ADVANTAGE - (I) is a synthetic nucleotide **analog** which is resistant to **nuclease**.
Dwg.0/21

L30 ANSWER 9 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-281436 [29] WPIDS
DNN N2001-200692 DNC C2001-085512
TI Screening **assays** for used for identifying compounds having a physiological effect on proteins identified as being essential.
DC B04 C07 D16 S03
IN DAVIES, R W; KAISER, K; YANG, M Y
PA (UNIU) UNIV GLASGOW
CYC 95
PI WO 2001018547 A1 20010315 (200129)* EN 695p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000070245 A 20010410 (200137)
EP 1212620 A1 20020612 (200239) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

ADT WO 2001018547 A1 WO 2000-GB3444 20000906; AU 2000070245 A AU 2000-70245 20000906; EP 1212620 A1 EP 2000-958829 20000906, WO 2000-GB3444 20000906
FDT AU 2000070245 A Based on WO 200118547; EP 1212620 A1 Based on WO 200118547
PRAI GB 1999-21009 19990907
AB WO 200118547 A UPAB: 20010528
NOVELTY - A screening **assay** (M1) for identifying compounds which have a physiological effect on an organism comprises:

(a) reacting a test compound with a protein encoded by an essential gene (EG) comprising a sequence selected from (S1)-(S902) (their specific fragments, homolog), fully defined in the specification; and

(b) detecting any modulatory effect the compound has on the protein.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) selectively modulating (M2) activity of a protein encoded by an EG comprising administering a compound that selectively modulates activity of the protein in the organism;

(2) a compound (I) with modulatory activity on a protein encoded by an essential gene;

(3) use of (I) as a pesticide;

(4) selectively modulating the in vivo activity of a protein encoded by an essential gene selected from (S1)-(S902) comprising administering a compound that selectively modulates the activity of the protein in the organism;

(5) an isolated polynucleotide (II) fragment comprising a sequence consisting of (S430)-(S783) and (S899)-(S902), (a fragment or variants of these);

(6) an expression vector (III) comprising an essential gene selected from (II);

(7) a prokaryotic or eukaryotic host cell comprising (III);

(8) producing (M3) a polypeptide by culturing (III);

(9) a polypeptide (IV) produced by (M2);

(10) modulating (M4) activity of a protein encoded by an EG, comprising administering a compound (C1), where the ability of the protein to modulate the activity of the protein is determined by:

(a) exposing the protein which has been produced by a genetically engineered cell expressing the protein, with C1 for a period of time;

(b) measuring the activity of the exposed protein using a ligand binding or functional activity **assay**; and

(c) comparing the activity of the exposed protein with an activity of a control protein which has not been exposed to C1, so that compounds that modulate the protein activity, are identified;

(11) Identifying (M5) compounds (C2) having a potentially pesticidal activity caused by modulation of a protein encoded by an EG, comprises:

(a) obtaining the protein by heterologous expression of the essential gene in a host cell;

(b) employing the protein in an **assay** for detecting C2 which displays modulatory activity on the protein; and

(c) testing C2 which displays modulatory activity on the protein for its pesticidal activity on an organism.

USE - (I) and C1 are useful as pesticides. Furthermore, in conjunction with other pesticides, herbicides and agriculturally usual auxiliaries they are used as crop protection material.

(II) Is useful for identifying and facilitating:

(i) the isolation an essential gene;

(ii) the isolation of homologous sequences from other organisms; and

(iii) the isolation of genes, from other organisms comprising homologous sequences.

(IV) Is useful in an **assay** for identifying a compound which modulates activity of (IV).

Dwg.0/0

TECH UPTX: 20010528
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred **Assay**: The sequence selected in M1 is preferably (S430)-(S783) and (S899)-(S902), and the effect of on the protein is a negative modulation.
M1 is either:
(a) a ligand **binding assay** for **detecting** the effect the compound has on the ligand binding activity of the protein; or
(b) a functional **assay** for **detecting** the effect the compound has on the functional activity of the protein.
The functional activity **assay** is selected from kinsmen **assays**;protein phosphatase **assays**; adenyl cyclase **assays**; guanylyl cyclase **assays**; phosphodiesterase **assays**; **nucleosidase assays** ; protease **assays**; protein secretion and/or import **assays**; **nuclease assays**; DNA metabolism **assays**; transcription factor **assays**; apoptosis **assays**; calcium utilization **assays**; receptor/ion channel **assays**; and G protein **assays**.
Preferred Method: In M2, the selective modulation in activity of the protein has the result of substantially eliminating or severely reducing the activity of the protein, as compared to the activity of the protein without modulation. The modulating compound has a minimal effect on other proteins of the organism. Furthermore, the modulation in activity has the effect of being lethal or semi-lethal to the organism.
(M4) Further included selectively modulating activity of a protein comprising:
(a) exposing a further cellular protein(s) to the compound for a period of time;
(b) measuring the activity of the further protein(s) using an **assay**(s); and
(c) comparing the activity of the exposed further cellular protein(s) with an activity of a control protein(s) which has not been exposed to the compound, so that compounds that modulate the further cellular protein(s) activity, are identified.
The compound (C1) identified in the above method has pesticidal activity.
Preferred Vector: (III) Further comprises one or more control sequences capable of directing the replication and/or expression of an operatively linked EG.

L30 ANSWER 10 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-125475 [14] WPIDS
CR 1992-425695 [52]; 1998-288704 [26]
DNC C2001-036597
TI New synthetic catalytic oligonucleotide structure useful for cleaving target nucleic acid sequences, e.g. for treating viral infections, comprises 2'-O-alkyl nucleotides outside of the catalytic center.
DC B04 C03 D16
IN LAMOND, A; PAOLELLA, G; SPROAT, B
PA (EMBL-N) EMBL EURO LAB MOLEKULARBIOLOGIE
CYC 15
PI EP 1061085 A2 20001220 (200114)* DE 14p
R: AT BE CH DE DK ES FR GB IT LI LU MC NL PT SE
ADT EP 1061085 A2 Div ex EP 1992-110298 19920617, Div ex EP 1997-121976 19920617, EP 2000-117112 19920617
FDT EP 1061085 A2 Div ex EP 519463, Div ex EP 845476
PRAI DE 1992-4216134 19920515; DE 1991-4120406 19910620
AB EP 1061085 A UPAB: 20010312
NOVELTY - Synthetic catalytic oligonucleotide structure (I) comprising nucleotide units having a hydroxy or alkoxy group in the 2' position, provided that the nucleotide units in the catalytically active center have

2'-hydroxy groups, is new (N.B. it is implied but not stated that the other nucleotide units have 2'-alkoxy groups).

DETAILED DESCRIPTION - Synthetic catalytic oligonucleotide structure (I) comprising at least one nucleotide of formula (II) is new:

B' = a nucleobase;

V' = O or CH2;

X, W' = O, S, NH2, 1-10C alkyl or 1-10C alkoxy; and

R = H or 1-10C alkyl; provided that the nucleotides in the catalytically active center have

R = H.

INDEPENDENT CLAIMS are also included for the following:

(1) a method for cleaving a target nucleic acid sequence using (I);

(2) a medicament comprising (I) and optionally carriers, excipients, fillers and/or diluents;

(3) a diagnostic reagent containing (I) as a component;

(4) a catalytic hammerhead oligonucleotide of formula (III);

(5) a catalytic hammerhead oligonucleotide of formula (IV); and

(6) use of (III) or (IV) to cleave a target nucleic acid sequence of formula (V):

N, N0-N14 = nucleotides of formula (II); provided that in;

N1, N4, N8, N10 and N11, R = H; and in N2, N3, N5, N6, N7, N9, N12, N13 and N14;

R = alkyl; and that N5 and N6 are complementary to each other;

x = 1 or more;

y = 2 or more;

N', N = (a) two nucleotide sequences consisting at least partly of complementary nucleotides to provide stable base pairing between the sequences; or

together, N' and N = a single nucleotide sequence, at least part of which can form a double-stranded stem through base pairing of complementary nucleotides;

M = a chemical bond or a nucleotide sequence (N)a;

a, m, n = 1 or more

U = **uridine**;

Z = A, C or U;

K, Y = any nucleotides; and

b = 3 or more.

ACTIVITY - Gene therapy; anti-HIV; virucide.

MECHANISM OF ACTION - Nucleic acid cleavage.

USE - (I) is useful for cleaving target nucleic acid (especially RNA) sequences, especially for treating viral infections in humans, animals and plants, especially acquired immunodeficiency syndrome (AIDS), and as a diagnostic reagent for use in genetic analysis procedures.

ADVANTAGE - Catalytic oligonucleotide structures with 2'-alkoxy substituents outside the catalytic center have better nuclease resistance than native RNA structures (no data given for structures with R = alkyl).

Dwg.0/0

TECH UPTX: 20010312

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Structure (I): This has a hammerhead or hairpin structure, optionally with 3'-deoxyribonucleotide and/or 3'-O-alkylribonucleotide units at the 3' ends. (I) can contain nucleotides whose nucleobases are modified with a crosslinker, especially sporalen or a psoralen derivative. (I) can be linked to a **prosthetic** group selected from polyamino acids, lipids, hormones and peptides to enhance cellular uptake and/or specific cellular localization.

Preferred Method (1): The target nucleic acid sequence is an RNA sequence. Cleavage is effected in the presence of a divalent (especially magnesium) cation at pH 7-9.

L30 ANSWER 11 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-007201 [01] WPIDS
CR 2002-075152 [10]
DNC C2001-001816
TI Detecting a DNA sequence, particularly a single nucleotide polymorphism using a pair of nucleotide sequences, a primer and an snp detection sequence having an electrophoretic tag.
DC B04 D16
IN SINGH, S; SALIMI-MOOSAVI, H; XIAO, V; CHENNA, A; MATRAY, T; TIAN, H
PA (ACLA-N) ACLARA BIOSCIENCES INC; (SALI-I) SALIMI-MOOSAVI H; (SING-I) SINGH S; (XIAO-I) XIAO V; (CHEN-I) CHENNA A; (MATR-I) MATRAY T; (TIAN-I) TIAN H
CYC 93
PI WO 2000066607 A1 20001109 (200101)* EN 76p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000044972 A 20001117 (200111)
US 6322980 B1 20011127 (200175)
US 2001049105 A1 20011206 (200203)
US 2001051340 A1 20011213 (200204)
US 2002001808 A1 20020103 (200207)
US 2002009737 A1 20020124 (200210)
US 2002015954 A1 20020207 (200213)
EP 1180112 A1 20020220 (200221) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002045738 A1 20020418 (200228)
US 2002058263 A1 20020516 (200237)
US 2002090616 A1 20020711 (200248)
ADT WO 2000066607 A1 WO 2000-US11396 20000428; AU 2000044972 A AU 2000-44972 20000428; US 6322980 B1 US 1999-303029 19990430; US 2001049105 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-824984 20010402; US 2001051340 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-824851 20010402; US 2002001808 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-825247 20010402; US 2002009737 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-824905 20010402; US 2002015954 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-825246 20010402; EP 1180112 A1 EP 2000-926444 20000428, WO 2000-US11396 20000428; US 2002045738 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-825245 20010402; US 2002058263 A1 Cont of US 1999-303029 19990430, US 2001-824861 20010402; US 2002090616 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-825244 20010402
FDT AU 2000044972 A Based on WO 200066607; EP 1180112 A1 Based on WO 200066607; US 2002090616 A1 Cont of US 6322980
PRAI US 1999-303029 19990430; US 2000-561579 20000428; US 2000-602586

20000621; US 2000-684386 20001004; US 2000-698846 20001027; US 2001-824984 20010402; US 2001-824851 20010402; US 2001-825247 20010402; US 2001-824905 20010402; US 2001-825246 20010402; US 2001-825245 20010402; US 2001-824861 20010402; US 2001-825244 20010402

AB WO 200066607 A UPAB: 20020730

NOVELTY - DNA sequence in a target nucleic acid sample is detected by executing primer extension in the presence of a polymerase, target DNA (TA) and a reagent pair consisting of a primer which specifically **binds** to TA and **detection** sequence (DS) comprised of nucleotide bases for each DNA sequence to be determined that binds to TA downstream from primer and has an electrophoretic tag specific for each DNA sequence.

DETAILED DESCRIPTION - The above method (I) comprises:

(a) combining under primer extension conditions, a polymerase having 5' to 3' exonuclease activity, TA and a reagent pair consisting of a primer and DS comprising of nucleotide bases for each DNA sequence to be determined, where each primer specifically binds to TA and DS binds to TA downstream from the primer in the direction of primer extension and has a electrophoretic tag specific for each DNA sequence;

(b) executing at least 1 cycle of the primer extension, where DS bound to target DNA is at least partially degraded with release of the electrophoretic tag free of the detection sequence;

(c) separating released electrophoretic tags into individual fractions; and

(d) detecting the fractions using the tag, where the presence of the DNA sequence in the TA sample is detected, provided that, when separation is performed solely by differences in mass, the electrophoretic tags that are separated all have the same number of nucleotides bonded to the electrophoretic tag.

INDEPENDENT CLAIMS are also included for the following:

(1) determining (II) the amount of at least 1 single nucleotide polymorphism (snp) in a target DNA sample, comprising:

(a) combining with step (a) of (I), a quantitating system comprising at least 2 control sequences having a common primer region and different control detection regions downstream from the primer region in the direction of primer extension, a primer sequence complementary to the primer region and a control DS for each of the control detection regions characterized by having a labeled electrophoretic tag specific for the control DS to which it is bound;

(b) executing at least 1 cycle of primer extension, where snp DS is bound to TA and control DS are partially degraded with release of electrophoretic tags;

(c) electrophoretically separating the tags into separate bands and determining the signal from the label from each of the bands; and

(d) comparing the band signal from control DS with signals from snp DS;

(2) a **kit** comprising several snp detection sequences characterized by consisting of at least 12 nucleotides, the 5' nucleotide bonded to an electrophoretic tag, the penultimate nucleotide bonded to the adjacent nucleotide by a link resistant to exonuclease hydrolysis and a complementary nucleotide to a snp at other than the terminal nucleotide; and

(3) a **kit** comprising several compounds of the formula: R-L-T, where R is a fluorescer, L is a linking group selected from NH-lysine, NH-(lysine)2, NH-alanine, NH-aspartic acid, NH-(aspartic acid)2, NH-(aspartic acid)3, NH-(aspartic acid)4, NH-(aspartic acid)5, NH-(aspartic acid)6, NH-(aspartic acid)7, NH-alanine-lysine, NH-aspartic acid-lysine, NH-(aspartic acid)2-lysine, NH-(aspartic acid)3-lysine, NH-(aspartic acid)4-lysine, NH-(aspartic acid)5-lysine, NH-(aspartic

acid)6-lysine, NH-(aspartic acid)7-lysine, NH-(aspartic acid)8-lysine, NH-(lysine)4 and NH-(lysine)5 and T is selected from a purine, pyrimidine, **nucleoside**, nucleotide, and nucleotide triphosphate.

USE - The method is useful for detecting at least 1 nucleic acid sequence or several snps in a target DNA sample.

ADVANTAGE - The method provides an improved analysis of complex nucleic acid mixture and for simultaneous identification of several entities such as sequences, snps, alleles, mutations, etc.

Dwg.0/9

TECH UPTX: 20001230

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: Several pairs are combined for **determining** many snps in the target DNA, where the **detection** sequences **bind** at the site of the snps. The **detection** sequence comprises a linkage resistant to exonuclease hydrolysis, between the second and third bases and optionally successive bases in the direction of degradation. (I) further comprises the additional step of reacting the electrophoretic tag with a fluorophore after release of the tag. The tag comprises a neutral or charged linker of 1-60 carbon atoms. The snp DS further comprises a quencher which quenches fluorophore when bound to the snp DS and further includes monitoring the change in fluorescence during the execution of primer extension. The snp **detection** sequences are within 200 nucleotides of the primer when bound to the target DNA and comprises positively charged groups such as lysine, arginine or histidine. The improvement in (I) comprises providing a mixture of E-TAGs having the same number of nucleotides bound to the E-TAGs by the E-TAGs having the penultimate linkage and optionally successive linkage of DS **nuclease** resistant to hydrolysis. The E-TAGs are labeled at the penultimate or terminal nucleotide with a label that binds to a positively charged receptor and includes the additional step of combining the released E-TAGs with the positively charged receptor and separating the E-TAGs into fractions by electrophoresis or using the receptor. In (II) at least 3 different control sequences are employed with the respective control **detection** sequences and the concentration of each control sequence differs by at least the factor of 100 from another control sequence. The control sequences comprises a linkage, resistant to exonuclease hydrolysis between the second and third bases in the direction of degradation.

Preferred Tag: The electrophoretic tag comprises a fluorophore or an amino acid or a peptide such as lysine, arginine or histidine.

L30 ANSWER 12 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2000-672835 [65] WPIDS
DNC C2000-203848
TI Sequence analysis of target nucleic acids for clinical and public health studies, such as diagnosing genetic diseases, comprises comparing mass spectra of the target nucleic acids with a known reference to detect sequence differences.
DC B04 D16
IN STANSSENS, P; ZABEAU, M
PA (METH-N) METHEXIS NV
CYC 91
PI WO 2000066771 A2 20001109 (200065)* EN 103p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000055236 A 20001117 (200111)
EP 1173622 A2 20020123 (200214) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 2001005293 A 20011220 (200221)
ADT WO 2000066771 A2 WO 2000-EP3904 20000430; AU 2000055236 A AU 2000-55236 20000430; EP 1173622 A2 EP 2000-940234 20000430, WO 2000-EP3904 20000430; NO 2001005293 A WO 2000-EP3904 20000430, NO 2001-5293 20011029
FDT AU 2000055236 A Based on WO 200066771; EP 1173622 A2 Based on WO 200066771
PRAI US 1999-131984P 19990430
AB WO 200066771 A UPAB: 20001214
NOVELTY - Sequence analysis (M1) of target nucleic acids (NA) for which a reference NA is known comprises cleaving the NA's, performing mass spectroscopy on the products, comparing the mass spectra with that of the known reference, deducing the sequences of the targets by systematic computational analysis and comparing with the reference to determine similar or different sequences.

DETAILED DESCRIPTION - Sequence analysis (M1) of one or more target NA's for which a reference NA sequence is known comprises:

(a) deriving the target NA's from biological samples;

(b) subjecting the target NA's to complementary cleavage reactions with reagents to generated cleavage products;

(c) performing mass spectroscopical analysis on the cleavage products to obtain one or more mass spectra; and

(d) comparing the mass spectra of the cleavage products of the target NA's in (c) with a known or predicted mass spectra for the reference NA sequence;

(e) deducing by systemical computational analysis the nucleotide sequence of the target NAs; and

(f) comparing the deduced sequences with the reference NA to determine the same or different sequences.

INDEPENDENT CLAIMS are also included for the following:

(1) scoring (M2) known nucleotide variations of target NA's for which a known reference NA is available comprising (a) - (c) of M1, comparing the spectra of the target NAs with the reference NA's and scoring by systemical computational analysis for the presence and absence of known nucleotide sequence variations of the target NA's;

(2) determining (M3) the sequence of one or more target NA's comprising performing systemical computational analysis on the mass spectra of cleavage products of the NA's;

(3) genome wide genotyping (M4) of unknown target NA's comprises (a) - (c) of M1, comparing the mass spectra of the cleavage products with reference mass spectra and diagnosing genetically relevant NA sequence variations of the unknown target NA's;

(4) identifying (M5) target NA's in biological samples comprising (a) - (c) of M1, comparing the mass spectra with each other or with mass spectra of reference NA's and deducing the identity of the target NA's; and

(5) a **kit** for sequence analysis of target NA's using mass spectroscopy comprising:

(i) sets of reference NA's for which the NA sequence is known;

(ii) nucleotide triphosphates;

(iii) nucleic acid cleaving agents; and

(iv) computer software for comparing mass spectra of target NA's with mass spectra of the reference NA's and deducing the NA sequence of the target NA.

USE - The new methods are used to analyze the sequences of target NA's, detect nucleotide variations, score genome-wide disease-associated mutations, and identify NA's in biological samples (claimed). Genetic diversity in molecular evolution can be studied using the new methods. The methods can be used for clinical and public health studies and can be used to diagnose more than 3000 genetic disease (e.g. hemophilias,

thalassemias, Duchenne Muscular Dystrophy, Huntington's disease, Alzheimer's disease and cystic fibrosis. They can also be used to diagnose predispositions to conditions, such as diabetes, atherosclerosis, obesity, autoimmune diseases and cancers.

ADVANTAGE - The new methods are more suited for the analysis of two or more non-contiguous target regions from a single biological sample, the analysis of heterozygous samples, and the simultaneous sequencing of analogous regions derived from different biological samples, than conventional methods. The methods can be tuned (by reducing complementary cleavage reactions) to limit the diagnostic sequencing to particular positions in a target NA.

Dwg.0/9

TECH UPTX: 20001214

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: In M1 and M2, the target NA is derived using modified **nucleoside** triphosphates that are mass modified deoxynucleoside triphosphates, dideoxynucleoside triphosphates, or ribonucleoside triphosphates. The **nucleoside** triphosphates are modified on the base, sugar, and/or phosphate moiety by an enzymatic step, chemically or by both. The modification consists of 2' substituents other than a hydroxyl group on the nucleotide triphosphates, phosphorothioate internucleoside linkages or phosphorothioate internucleoside linkages further reacted with an alkylating reagent, or a methyl group on C5 of the **uridine**-5'-monophosphate subunits. The modifications alter the specificity of cleavage by the reagents, the mass and/or the length of the cleavage products. The complementary cleavage reactions are enzymatic, chemical or physical cleavage and are characterized by a relaxed mono-nucleotide, mono-nucleotide, relaxed di-nucleotide, or di-nucleotide specificity. The chemical cleavage reaction consists of an alkali treatment.

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In M1 and M2, the NA sequence difference that is **determined** is a deletion, substitution, insertion or combinations of them. The biological sample is derived from eukaryotes, prokaryotes or viruses. The NA is single stranded DNA, double stranded DNA, cDNA, single stranded RNA, double stranded RNA, a DNA/RNA hybrid, or DNA/RNA mosaic NA. The target NA's are derived by consecutive amplification procedures that are in vivo cloning, polymerase chain reaction (PCR), reverse transcription followed by PCR (RT-PCR), strand displacement amplification (SDA), or transcription based processes. The target NA's are transcripts generated from a single or double stranded target NA by linking expression control sequences to the target NA's and transcribing the strands of the target NA's using RNA polymerases that recognize the transcription control sequence on the target NA's. The transcription control sequence is eukaryotic, prokaryotic, i.e. T3, T7 or SP6 promoters, or viral. The RNA polymerases which utilize the T3, T7, or SP6 promoters are either wild type or mutant RNA polymerases, the mutant polymerases being able of incorporating the RNA transcript non-canonical substrates with a 2'-substituent other than a hydroxyl group. The target NA is derived using modified **nucleoside** triphosphates that are mass modified deoxynucleoside triphosphates, dideoxynucleoside triphosphates, or ribonucleoside triphosphates. The modified **nucleoside** triphosphates are modified on the base, sugar, and/or phosphate moiety and are introduced through an enzymatic step, chemically or both. Enzymatic cleavage is performed using endonucleases, i.e. restriction enzymes, selective or non-selective RNA endonucleases, DNA endonucleases or non-specific phosphodiesterases, or exonucleases. The RNA endonucleases are G-specific T1 ribonuclease, A-specific U2 ribonuclease, A/U specific phyM ribonuclease, U/C specific ribonuclease A, C-specific chicken liver ribonuclease (RNaseCL3) or cusativin. The target NA are

phosphorothioate-modified single-stranded DNA or RNA and the endonuclease is **nuclease** P1. The mass spectroscopical **analysis** is performed using a mass spectroscopic method that is Matrix-Assisted Laser Desorption/Ionization-Time-of-flight (MALDI-TOF), Electrospray-Ionization (ESI), and Fourier Transform-Ion Cyclotron Resonance (FT-ICR). In M5, the target NA's are cDNA. The method is used to **determine** an expression profile in a biological sample.

L30 ANSWER 13 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2000-565376 [52] WPIDS
DNC C2000-168423
TI **Detection** of **nuclease** enzymes useful in nucleic acid hybridization **assays**, enzyme **immunoassays** and ligand receptor binding **assays** by contacting with a 3' **nucleosidyl** derivative, a **phospho radical** and an esterifiable moiety or H.

this applica

DC B04 D16
IN HARBRON, S
PA (HARB-I) HARBRON S; (ZETA-N) ZETATRONICS LTD
CYC 91
PI WO 2000049172 A1 20000824 (200052)* EN 23p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
GB 2347213 A 20000830 (200052)
AU 2000025656 A 20000904 (200103)
GB 2347213 B 20010627 (200137)
EP 1155143 A1 20011121 (200176) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000049172 A1 WO 2000-GB606 20000221; GB 2347213 A GB 1999-3851 19990220; AU 2000025656 A AU 2000-25656 20000221; GB 2347213 B GB 1999-3851 19990220; EP 1155143 A1 EP 2000-903907 20000221, WO 2000-GB606 20000221
FDT AU 2000025656 A Based on WO 200049172; EP 1155143 A1 Based on WO 200049172
PRAI GB 1999-3851 19990220
AB WO 200049172 A UPAB: 20001018
NOVELTY - **Detecting** a **nuclease** enzyme comprising contacting the enzyme with RpX, where R is a 3'**nucleosidyl** derivative, p is a **phospho radical** and X is an esterifiable moiety or, when R is a 3'**nicotinamide** derivative, X is an esterifiable moiety or H, to produce ROH and pX, and **detecting** the pX moiety, or if R is a 3'**nicotinamide** derivative, **detecting** the pX or ROH moiety, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) **detecting** a **nuclease** enzyme, comprising contacting the enzyme with a phosphodiester comprising a **prosthetic** group and a 3'**nucleoside** causing production of the **prosthetic** group, and **detecting** the **prosthetic** group;

(2) **detecting** a **nuclease** enzyme, comprising contacting the enzyme with RpX, where R is a 3'**nicotinamide** derivative, p is a **phospho radical**, and X is an esterifiable moiety causing ROH and pX production, and **detecting** the ROH moiety; and

(3) a **kit** for **detecting** the presence of a

nuclease enzyme comprising:
(a) RpX, where R is a 3'**nucleosidyl** derivative, p is a **phospho radical**, and X is an esterifiable moiety or, if R is 3'**nicotinamide** derivative, X is an esterifiable moiety or H; and
(b) a detection system for detecting pX or, if R is 3'**nicotinamide** derivative, a detection system for detecting pX or ROH.
USE - The method is useful for **detecting** a **nuclease** enzyme that is free in solution, immobilized on a surface or attached to a member of a specific binding pair (claimed). The **nuclease** enzyme may be attached to one of a binding pair and used to **detect binding** events between the pair e.g. an antibody and an antigen or a nucleic acid probe and its corresponding target sequence. It may be applied as a **detection** step in nucleic acid hybridization **assays**, enzyme **immunoassays** and ligand:receptor binding **assays**.
Dwg.0/6

TECH UPTX: 20001018
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Methods: The 3' **nucleoside** is **adenosine**, cytosine, guanine, **thymidine** or **uridine** (or derivatives), pX is a **prosthetic** group, especially **riboflavin** 5' phosphate, **pyridoxal** phosphate, **pyridoxamine** phosphate or thiamine **pyrophosphate**, or its derivatives, in this case detection is by contacting the **prosthetic** group with an **apoenzyme** preferably an apoglycolate oxidase or a transaminase. Alternatively, X may be a 1,2-**dioxetane** compound and detection is by contacting the 1,2,-**dioxetane** phosphate produced with a phosphatase enzyme and detecting light production.
Preferred Method: Detection is by conducting enzymatic cycling of **NAD-NADH** interconversions using **dehydrogenase**, a **dehydrogenase** substrate, a **tetrazolium** dye and a **diaphorase**, and quantifying **NAD** or **NADH** by the color-development signal of formazan produced by the action of **diaphorase** and **NADH-NAD** conversions.
Preferred **Kit**: RpX is **NAD3P**, **NAD3PH**, **nucleoside**-3'phosphoriboflavin derivative, **nucleoside** -3'-phospho-**pyridoxal** derivative, **nucleoside** -3'-phospho-**pyridoxamine** derivative, **nucleoside** -3'-phospho-thiamine derivative, or **nucleoside** -3'-phospho-1,2-dioetane derivative. The detection system comprises a **dehydrogenase**, a **diaphorase** and a **tetrazolium** compound. Alternatively, the detection system comprises an **apoenzyme** or a phosphatase.

L30 ANSWER 14 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2000-482973 [42] WPIDS
DNC C2000-145405
TI New isolated nucleic acid useful for screening **assays** to identify compounds capable of regulating beta3-AR (adrenergic receptor) expression, is composed of three regulatory segments.
DC B04 D16
IN DUZIC, E; SUSULIC, V S
PA (AMHP) AMERICAN HOME PROD CORP
CYC 90
PI WO 2000044901 A1 20000803 (200042)* EN 78p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES

FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000027507 A 20000818 (200057)
US 6197580 B1 20010306 (200115)
EP 1147191 A1 20011024 (200171) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002102552 A1 20020801 (200253)

ADT WO 2000044901 A1 WO 2000-US2632 20000201; AU 2000027507 A AU 2000-27507 20000201; US 6197580 B1 US 1999-243335 19990201; EP 1147191 A1 EP 2000-905905 20000201, WO 2000-US2632 20000201; US 2002102552 A1 Div ex US 1999-243335 19990201, US 2001-761116 20010116

FDT AU 2000027507 A Based on WO 200044901; EP 1147191 A1 Based on WO 200044901

PRAI US 1999-243335 19990201; US 2001-761116 20010116

AB WO 200044901 A UPAB: 20000905

NOVELTY - An isolated nucleic acid (I) comprising a nucleotide sequence that is greater than 80% identical to the fully defined 12 nucleotide sequence, is new.

DETAILED DESCRIPTION - An isolated nucleic acid (I) comprising a nucleotide sequence that is greater than 80% identical to the nucleotide sequence GCCTCTGGGGAG, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid (II) comprising a nucleotide sequence AGGTGGGACT, which is 5' to a sequence GCCTCTGGGGAG, which is 5' to about 20 repeats of a sequence CCTT;

(2) a nucleic acid (III) that hybridizes under conditions of high stringency to (I) having the sequence GCCTCTGGGGAG;

(3) a cell line (IV) containing (I) or (II);

(4) a beta 3-AR (adrenergic receptor) trans-activating factor polypeptide (V) having the following characteristics:

(a) it binds specifically to (I);

(b) it is expressed by brown adipose tissue cells;

(c) it is expressed at very low levels by cells isolated from the perirenal depot;

(d) an AP-2 binding nucleic acid does not compete with (I) for binding the polypeptide; and

(e) when complexed to (I), it is not recognized by an antibody to AP-2;

(5) isolating (V); and

(6) a method (VI) for screening for compounds that increase or decrease activity of a beta 3-AR trans-activating factor in human cells, comprising contacting cells capable of producing beta 3-AR trans-activating factor with a test compound and detecting an increase or decrease in the level of activity.

USE - Recombinant vectors under control of the transcription regulation region comprising (II) provide a substrate for high throughput **assays**, particularly reporter gene **assays** to identify compounds capable of increasing or decreasing the level of expression of beta 3-AR (claimed). (II) can be used for regulating gene expression and for drug screening. It is envisaged that beta 3-AR stimulation may have beneficial effects in the treatment of obesity and type II diabetes.

Dwg.0/7

TECH UPTX: 20000905

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Isolation: (V) is isolated by contacting a composition suspected of containing the polypeptide with (I) under conditions that permit **detection** of **binding** of the polypeptide to the nucleic acid and isolating the bound polypeptide. The composition is a yeast hybrid **assay** system recombinantly engineered to express polypeptides from cells that express beta3-AR or is

a nuclear extract from cells that endogenously express beta3-AR. The cells are selected from human brown adipose tissue cells, human neuroblastoma cells and HIB cells.
Preferred Nucleic Acid: The nucleotide sequence in (I) is preferably GCCTCTGGGGAG and (I) further comprises a nucleotide sequence that binds an Sp-1 transcription factor protein and an S1 **nuclease** sensitive site. In (II), the nucleic acid sequences are approximately 7 kb genomic nucleic acid upstream of a beta3-AR transcription initiation site. (II) also comprises a gene, preferably a reporter gene, operatively associated with a promoter downstream of the trans-activator binding site and the S1 **nuclease** sensitive site.
Preferred Promoter: The promoter in (II) is a herpes simplex virus **thymidine** kinase minimum promoter or a beta3-AR promoter.
Preferred Method: In (VI), the increase or decrease in the level of activity of the beta3-AR trans-activating factor is **detected** by **detecting** an increase or decrease in the level of expression of the reporter gene operatively associated with a nucleic acid sequence having the sequence GCCTCTGGGGAG relative to a level of expression prior to contact with the test compound. Alternatively, the increase or decrease is **detected** by **detecting** an increase or decrease in the amount of beta3-AR trans-activating factor present in the cells after contacting them with the test compound. When screening for a compound that increases activity, the cells do not endogenously express, or express at a very low level, beta3-AR and are selected from HeLa, CV and WAT (White Adipose Tissue) cells. When screening for a compound that inhibits activity, the cells endogenously express beta3-AR and are neuroblastoma or BAT (Brown Adipose Tissue) cells.

L30 ANSWER 15 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 2000-350762 [30] WPIDS
DNC C2000-106788
TI Detecting nucleic acid amplification products from target-dependent amplification processes involving probes and/or primers, useful in molecular biology.
DC B04 D16
IN HARBRON, S
PA (HARB-I) HARBRON S; (ZETA-N) ZETATRONICS LTD
CYC 91
PI WO 2000024930 A1 20000504 (200030)* EN 27p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
GB 2346145 A 20000802 (200038)
AU 9963551 A 20000515 (200039)
GB 2346145 B 20010124 (200107)
EP 1123416 A1 20010816 (200147) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2002051983 A1 20020502 (200234)
ADT WO 2000024930 A1 WO 1999-GB3510 19991022; GB 2346145 A GB 1999-25120 19991022; AU 9963551 A AU 1999-63551 19991022; GB 2346145 B GB 1999-25120 19991022; EP 1123416 A1 EP 1999-950964 19991022, WO 1999-GB3510 19991022; US 2002051983 A1 US 2001-840499 20010423
FDT AU 9963551 A Based on WO 200024930; EP 1123416 A1 Based on WO 200024930
PRAI GB 1998-23005 19981022
AB WO 200024930 A UPAB: 20000624
NOVELTY - A method (I) for **detecting** nucleic acid amplification

products of a target-dependent nucleic acid amplification process involving at least 1 probe or primer, is new. (I) comprises treating the product with a **nuclease** agent so that the product is hydrolyzed into its mononucleotide components and **detecting** the mononucleotide components.

USE - (I) is used for detecting nucleic acid amplification products from target-dependent amplification processes involving probes and/or primers.

ADVANTAGE - (I):

(1) provides a universal method for detecting nucleic acid amplification products (the same reagent may be used for detecting both polydeoxyribonucleotide and polyribonucleotide amplification products);

(2) can be performed without capturing or purifying the amplification products (the detection step may be performed in the same vessel as was used for amplification and the detection reaction is carried out in a homogenous format);

(3) is easy to use and only a moderate level of skill is required by the operator;

(4) is economical and uses components that are inexpensive and easily available from commercial suppliers; and

(5) is sensitive (hydrolysis of the amplification product increases the number of molecules to be detected (e.g. if the product was 400 bases long, a roughly 400-fold amplification is achieved by (I)).

Dwg.0/0

TECH UPTX: 20000624

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Methods: In (I) the product is a polydeoxyribonucleotide product when the target is RNA or a polyribonucleotide product when the target is DNA. The **nuclease** reagent is specific for polyribonucleotide or polydeoxyribonucleotide depending on the type of product. The probes and primers are **nuclease** resistant and comprise nucleic acid **analogs**.

The nucleic acid **analogs** comprise PNA (undefined) or PENAM (peptide-based nucleic acid mimics).

The target-dependent nucleic acid amplification process is selected from: RT-PCR (reverse transcription polymerase chain reaction (PCR)), PCR, SDA (undefined), TMA (undefined, preferred), NASBA (undefined, preferred). The mononucleotide components are converted to 5' ADP (**adenosine** diphosphate), which is **detected**. The conversion comprises a reaction catalyzed by a kinase from Enzyme Commission Class 2.7.4. and the ADP is **detected** by a method comprising:

(1) converting the 5' ADP to pyruvate using a pyruvate kinase in the presence of phosphophoenol pyruvate; and

(2) either:

(i) converting the pyruvate to hydrogen peroxide using a pyruvate oxidase in the presence of oxygen and phosphate and **detecting** the hydrogen peroxide; or

(ii) converting the pyruvate to lactate using a lactate **dehydrogenase** in the presence of **NADH** (reduced **nicotinamide** adenine dinucleotide) and **detecting** the hydrogen peroxide and **detecting** a change in the absorbancy of **NADH**.

The target-dependent nucleic acid amplification process comprises a step where the RNA portion of a DNA:RNA hybrid is hydrolysed to mononucleotide components by the **nuclease** reagent. The **nuclease** reagent is RNase H or an RNA polymerase that also has RNase H activity. The **nuclease** reagent is preferably non-specific and the target and product are hydrolyzed so that the mononucleotide components comprise deoxyribonucleotides and ribonucleotides. The **detection** step is specific for the deoxyribonucleotides if the product components comprise deoxyribonucleotides and/or ribonucleotides if the product components

comprise ribonucleotides.
In particular, the target is RNA and the product is a polydeoxyribonucleotide. For **detection** the polydeoxyribonucleotides are converted to 5' ADP by a kinase specific for deoxyribonucleotides. Alternatively, the target is DNA and the product is a polyribonucleotide. For **detection** the polyribonucleotides are converted to 5' ADP by a kinase specific for ribonucleotides.

L30 ANSWER 16 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 1999-590846 [50] WPIDS
CR 2000-549282 [49]; 2000-549283 [49]; 2000-558304 [49]; 2000-565377 [49]; 2000-565378 [49]; 2001-182784 [13]; 2002-024902 [74]; 2002-412825 [44]
DNC C1999-172464
TI Detection of nucleic acids and cellular materials, used for forensic, clinical and agricultural applications.
DC B04 C07 D16
IN LEIPPE, D M; LEWIS, M K; MANREKAR, M A; NELSON, L S; SHULTZ, J W; NELSON, M N; MANDREKAR, M A; NELSON, M A
PA (PROM-N) PROMEGA CORP; (LEIP-I) LEIPPE D M; (LEWI-I) LEWIS M K; (NELS-I) NELSON L S; (NELS-I) NELSON M A; (SHUL-I) SHULTZ J W
CYC 85
PI WO 9946409 A1 19990916 (199950)* EN 166p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN
AU 9930792 A 19990927 (200006)
US 6159693 A 20001212 (200067)
EP 1064400 A1 20010103 (200102) EN
R: CH DE FR GB IT LI SE
US 2001014451 A1 20010816 (200149)
US 6335162 B1 20020101 (200207)
JP 2002505889 W 20020226 (200219) 181p
US 6379898 B2 20020430 (200235)
ADT WO 9946409 A1 WO 1999-US5304 19990311; AU 9930792 A AU 1999-30792 19990311; US 6159693 A CIP of US 1998-42287 19980313, US 1999-252436 19990218; EP 1064400 A1 EP 1999-912413 19990311, WO 1999-US5304 19990311; US 2001014451 A1 Cont of US 1998-42287 19980313, US 2001-757132 20010109; US 6335162 B1 US 1998-42287 19980313; JP 2002505889 W WO 1999-US5304 19990311, JP 2000-535775 19990311; US 6379898 B2 Cont of US 1998-42287 19980313, US 2001-757132 20010109
FDT AU 9930792 A Based on WO 9946409; EP 1064400 A1 Based on WO 9946409; JP 2002505889 W Based on WO 9946409; US 6379898 B2 Cont of US 6335162
PRAI US 1999-252436 19990218; US 1998-42287 19980313; US 2001-757132 20010109
AB WO 9946409 A UPAB: 20020711
NOVELTY - New methods for the detection of nucleic acids use enzymatic reactions to generate readily detectable materials.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) A method (A) for interrogating the identity of a specific base in a nucleic acid (NA) sample comprises:
(a) providing at least one NA probe and a sample suspected of containing at least one target NA (tNA), where the NA probe is complementary to the tNA and comprises at least one predetermined nucleotide at an interrogation position, and where the tNA comprises at least one base to be identified;
(b) hybridizing the NA probe to the tNA to form a NA probe-tNA

complex, where the predetermined nucleotide at the interrogation position is aligned with the base to be identified in the tNA so that base pairing may occur;

(c) treating the NA probe-tNA complex under conditions such that the probe is depolymerized and releases nucleotides; and

(d) detecting the released nucleotide;.

(2) a method of discriminating between identical NAs in a sample comprising:

(a) providing a sample suspected of containing at least 2 tNAs, where the tNAs comprise a region of identity having a mismatch of at least a single nucleotide at a predetermined position;

(b) providing at least one NA probe which is complementary to the tNA region of identity and comprises at least one nucleotide at an interrogation position, where the nucleotide at the interrogation position is complementary to the nucleotide at the predetermined position of the region of identity of the tNA;

(c) hybridizing the NA probe to the tNA to form a NA probe-tNA complex, where the nucleotide at the interrogation position is aligned with the nucleotide at the predetermined position in the region of identity;

(d) treating the NA probe-tNA complex so that the probe is depolymerized and releases nucleotides; and

(e) detecting the released nucleotides;

(3) a **kit** containing reagents for **detecting** a NA of interest or **detecting nuclease** activity comprising a vessel containing a **nucleoside** diphosphate kinase (NDPK) and a NA substrate;

(4) a method of **detecting nuclease** activity, exonuclease activity in a sample;

(5) a method of detecting DNA in a reaction containing **pyrophosphate**, **adenosine** 5'-diphosphate (A5DP), or a combination, comprising:

(a) depolymerizing a DNA at terminal nucleotide by enzymatically cleaving the terminal internucleotide phosphodiester bond and reforming same with a **pyrophosphate** molecule to form a free deoxyribonucleoside triphosphate (dNTP) molecule according to the reaction: dNAn + PPi --> dNAn-1 + dNTP;

(b) enzymatically transferring terminal 5' phosphate groups from the dNTP molecules to A5DP molecules to form **adenosine** 5'-triphosphate (A5TP) according to the following reaction: dNTP asterisk + ADP --> dNTP + ATP asterisk , where P asterisk is the terminal 5' phosphate so transferred; and

(c) detecting the A5TP formed;

(6) a method of detecting polyadenylated mRNA in a reaction containing **pyrophosphate**;

(7) a method of selectively detecting poly(A) -mRNA in a reaction containing **pyrophosphate**, A5DP, or a combination, comprising:

(a) hybridizing a complementary oligo (dT) probe to poly(A) -mRNA to form a RNA-DNA hybrid;

(b) depolymerizing the oligo (dT) strand of the RNA-DNA hybrid at the terminal nucleotide by enzymatically cleaving the terminal internucleotide phosphodiester bond and reforming same with a **pyrophosphate** molecule to form a deoxythymidine 5'-triphosphate molecule according the following general reaction catalyzed by a reverse transcriptase: dTTn + PPi --> dTTn-1 + dTTP;

(c) enzymatically transferring terminal 5' phosphate groups from the deoxythymidine 5'-triphosphate molecules to A5DP molecules to form A5TP molecules according to the reaction: dTTP asterisk + ADP --> dTDP + ATP asterisk , where P asterisk is the terminal 5' phosphate so transferred; and

(d) detecting the A5TP formed;
(8) a method of detecting DNA in a reaction containing phosphoribosylpyrophosphate (PRPP), A5DP, or a combination;
(9) a method of detecting RNA in a reaction containing PRPP;
(10) a method for determining the presence and/or amount of cells and cellular material;
(11) a method of producing ATP molecules from a **nucleoside** triphosphate molecule in a reaction containing **adenosine** 5'-monophosphate (A5MP) molecules, high energy phosphate donor molecules, or a combination;
(12) a method of detecting DNA or RNA in a reaction containing pyrophosphate, A5MP and a high energy phosphate donor, or a combination.
USE - The methods can be used for the quantitation of nucleic acids in forensic, clinical and agricultural samples.
ADVANTAGE - The methods can provide for the detection of low amounts of NS and low numbers of cells or cellular materials. They can provide for the detection and discrimination between NAs from different species, or even from different alleles.
Dwg.0/0

TECH UPTX: 19991201
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Methods: The methods may comprise use of reagents such as e.g. **adenosine** 5' phosphate, luciferase and **NADH**. The methods further comprise identifying the base to be identified. The target nucleic acid is deoxyribonucleic acid or ribonucleic acid. The interrogation position of said first probe comprises a nucleic acid residue is selected from the group consisting of deoxyadenosine residues and **adenosine** residues, where the interrogation position of the second probe comprises a nucleic acid residue selected from the group consisting of **uridine** residues and deoxythymidine residues. The interrogation position of the third probe comprises a nucleic acid residue selected from the group consisting of deoxyguanosine and **guanosine** residues, and the fourth nucleic acid probe comprises a nucleic acid residue selected from the group consisting of deoxycytosine and cytosine residues.
The method of (1) further comprises using a first, second, third and fourth probe. The nucleic acid probe further comprises a 5' end and a 3' end, where the interrogation position is within ten bases of the 3' end. The depolymerization is catalyzed by a Klenow exo minus polymerase, Taq polymerase, AMV reverse transcriptase or MMLV reverse transcriptase. The detecting step further comprises quantitating **adenosine** 5' triphosphate. The detecting step uses luciferase and **NADH** detection systems.
In the method of (2), the first and second nucleic acids are alleles. The first nucleic acid if from a first species and the second nucleic acid is from a second species.

L30 ANSWER 17 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 1999-337376 [28] WPIDS
DNC C1999-099147
TI New oligonucleotides containing polycyclic, locked **nucleoside** analogs, useful e.g. as diagnostic probes or in antisense therapy.
DC B02 B03 B04 D16 P28
IN NIELSEN, P; WENGEL, J; GIERER, J T
PA (EXIQ-N) EXIQON AS; (EMEL) EMERSON ELECTRIC CO; (NIEL-I) NIELSEN P; (WENG-I) WENGEL J
CYC 83
PI WO 9914226 A2 19990325 (199928)* EN 268p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE

GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

AU 9890633 A 19990405 (199933)

EP 1015469 A2 20000705 (200035) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

CN 1279687 A 20010110 (200128)

MX 9905037 A1 20000901 (200139)

KR 2001030586 A 20010416 (200163)

NZ 503765 A 20020426 (200236)

US 2002068708 A1 20020606 (200241)#

JP 2002521310 W 20020716 (200261) 337p

ADT WO 9914226 A2 WO 1998-DK393 19980914; AU 9890633 A AU 1998-90633 19980914; EP 1015469 A2 EP 1998-942516 19980914, WO 1998-DK393 19980914; CN 1279687 A CN 1998-810955 19980914; MX 9905037 A1 MX 1999-5037 19990531; KR 2001030586 A WO 1998-DK393 19980914, KR 2000-702608 20000311; NZ 503765 A NZ 1998-503765 19980914, WO 1998-DK393 19980914; US 2002068708 A1 Provisional US 1997-58541P 19970912, Provisional US 1997-68293P 19971219, Provisional US 1998-71682P 19980116, Provisional US 1998-76591P 19980303, Provisional US 1998-83507P 19980429, Provisional US 1998-88309P 19980605, Provisional US 1998-94355P 19980728, US 1998-152059 19980911; JP 2002521310 W WO 1998-DK393 19980914, JP 2000-511775 19980914

FDT AU 9890633 A Based on WO 9914226; EP 1015469 A2 Based on WO 9914226; NZ 503765 A Based on WO 9914226; JP 2002521310 W Based on WO 9914226

PRAI DK 1998-982 19980728; DK 1997-1054 19970912; DK 1997-1492 19971219; DK 1998-61 19980116; DK 1998-286 19980303; DK 1998-585 19980429; US 1998-88309P 19980605; DK 1998-750 19980608; US 1998-88309 19980601; US 1998-152059 19980911

AB WO 9914226 A UPAB: 20020711

NOVELTY - Novel modified oligonucleotides (I) contain at least one locked **nucleoside** analog (LNA). Monomeric LNA's (II) are also new.

DETAILED DESCRIPTION - Oligomers (I), containing at least one LNA of formula (I'), and their basic salts and acid addition salts are new:

X = O, S, N(R'N), CR6R'6, OCR7R'7, CR6R'6O, SCR7R'7, CR6R'6S, N(R'N)CR7R'7, CR6R'N(RN) or CR6R'6-CR7R'7;

B' = H or OH; 1-4C alkyl, 1-4C alkoxy or 1-4C acyloxy (all optionally substituted); or nucleobase, DNA intercalator, photo- or thermo-chemically active group, chelating group, reporter or ligand;

P' = position for internucleoside linkage or a 5'-terminal group, optionally with the linkage or group substituted by R5;

one of R2, R'2, R3, R'3 = P'', i.e. an intranucleoside linkage or 3'-terminal group;

one or two pairs of non-geminal substituents R'1, R'2- R'7, R2, R3, R5-R7, R'N (other than P'') = biradical of 1-8 groups/atoms, i.e. CRaRb, CRa=CRa, O, Si(Ra)2, S. SO2, NRa or C(=Z);

Z = O, S or NRa;

Ra, Rb = H; optionally substituted 1-12C alkyl, 2-12C alkenyl or 2-12C alkynyl; OH, 1-12C alkoxy, 1-12C alkoxycarbonyl, 1-12C alkylcarbonyl, 2-12C alkenyloxy, COOH or CHO; aryl, aryloxycarbonyl, aryloxy or arylcarbonyl (or corresponding heteroaryl groups; all optionally substituted); NH2, CONH2 or amino(1-6C)alkylaminocarbonyl, all optionally N-substituted by 1 or 2 1-6C alkyl; carbamido, 1-6C alkanoyloxy, sulfono, 1-6C alkylsulfonyloxy, NO2, N3, SH, 1-6C alkylthio; halo, DNA intercalator, photo- or thermo-chemically active group, chelating group, reporter or ligand;

or two gem Ra, Rb may = optionally substituted CH2;

or two geminal or non-geminal Ra, Rb or any of the above R groups not involved in P', P'' or biradicals may = biradical as defined above;

R'1-R'7, R2, R3, R5-R7 (if not involved in P', P'' or biradicals) =

as for Ra, or in geminal pairs form O, S, NH or optionally substituted CH2 or together form a spiro biradical comprising 1-5C alkylene chain, optionally interrupted and/or terminated by O, S or NRN, or two adjacent (non-geminal) substituents complete a double bond;

RN, R'N (if not part of a biradical) = H or 1-4C alkyl;

provided that if LNA is bicyclic then:

(i) R2 and R3 are not together O-(CH2)x (x = 2 or 3);

(ii) R3 and R5 are not together (CH2)2-OCH2; and

(iii) R'6 does not form CH2with R'1 or R'4; and

if LNA is tricyclic then R3, R5 and R'5 do not together form CH2-CH(-)-CH2.

INDEPENDENT CLAIMS are also included for:

(a) oligonucleotides (Ia) containing at least one **nucleoside** analog (IIa) which increases the melting point (Tm), with a complementary DNA oligonucleotide by at least 2.5 deg. C or Tm with the complementary RNA oligonucleotide by at least 4 deg. C;

(b) novel LNA monomers of formula (II) and their salts;

(c) conjugates of (I) with a protein, amplicon, enzyme, polysaccharide, hapten, peptide or peptide nucleic acid; and

(d) a solid phase carrying LNA, optionally protected at 5'-hydroxy or in the nucleobase.

B'' = nucleobase, DNA intercalator, photo- or thermo-chemically active groups, chelating groups, reporters or ligands;

X' = O, S, NRN or CR6R'6;

one of R2, R'2, R3 and R'3 = Q';

Q, Q' = H or a wide range of substituents;

the R groups form biradicals or are selected from a wide range of substituents.

The full definitions are given in the DEFINITIONS (Full Definitions) Field.

ACTIVITY - Antiviral; antitumor.

MECHANISM OF ACTION - (I) bind specifically to complementary RNA and DNA sequences.

USE - (I) are used:

(i) to bind to target sequences in double-stranded DNA or RNA (by strand displacement or triplex formation);

(ii) as ribozymes;

(iii) as therapeutic antisense, antigene or gene activating agents, specifically for recruitment of RNase H;

(iv) diagnostically for isolation, purification, detection, identification, quantitation or capture of (synthetic) nucleic acid, e.g. as probes or primers;

(v) as aptamers for therapy, diagnosis, RNA-mediated catalytic processes and for specific binding to antibodies, drugs etc., including resolution of enantiomers;

(vi) for labeling, then separating, cells; and

(vii) to hybridize to non-coding RNA.

LNA are used in synthesis of (I); as therapeutic and diagnostic agents; to equalize the meting point of unmodified reference oligonucleotides and as enzyme substrates. Typical therapeutic applications are as antiviral and antitumor agents.

ADVANTAGE - (I) have increased specificity and/or affinity, i.e. higher melting point (Tm), for complementary RNA or DNA than oligomers not containing LNA, and are more resistant to nuclease.

The unmodified oligonucleotide d(GTGATATGC) had Tm for the sequence d(GCATATCAC) of 28 deg. C (in phosphate-buffered saline containing EDTA). The corresponding modified oligonucleotide, having all T replaced by 2'-O,4'-C-linked analog, had Tm 44 deg. C, under the same conditions.

Dwg.0/41

TECH UPTX: 19990719

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred oligomers: These contain 2-15000 residues, particularly 1-10000 LNA and 0-10000 natural **nucleosides** or analogs, with at least one LNA having B' = nucleobase. (I) may also include peptide-nucleic acid monomers or oligomers.
(Ia) increases Tm by at least 2.5N (N = number of LNA present), relative to native nucleic acid, but when hybridized to partially complementary nucleic acid, Tm of (I) is reduced by at least as much as that for the corresponding native oligonucleotide.
Preparation: Typically to produce a 2'-O,4'-C-linked LNA, a 4'-C-hydroxymethyl furanose of formula (31) is benzylated, acetylated, acetolysed and again acetylated; the obtained triacetyl compound is stereospecifically reacted with silylated thymine (or other bases) and deacetylated; the obtained diol of formula (35) is tosylated and the product cyclized and debenzylated to form the product of formula (37). This can be protected at the 5'-hydroxy position and converted to phosphoramidite conventionally.
(I) are produced by conventional methods of oligonucleotide synthesis.

L30 ANSWER 18 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 1998-377588 [32] WPIDS
DNC C1998-114700
TI **Nucleoside** and nucleotide derivatives with 2'-O-amino or oximino substituent(s) - or specific non-natural bases and oligo nucleotide(s), particularly ribozyme(s), that incorporate them, useful for treatment and diagnosis of disease.
DC B04 D16
IN BEIGELMAN, L; KARPEISKY, A; MATULIC-ADAMIC, J
PA (RIBO-N) RIBOZYME PHARM INC
CYC 23
PI WO 9828317 A2 19980702 (199832)* EN 105p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP MX
AU 9857204 A 19980717 (199848)
EP 948511 A2 19991013 (199947) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6159951 A 20001212 (200067)
US 6248878 B1 20010619 (200137)
US 6251666 B1 20010626 (200138)
JP 2001507688 W 20010612 (200139) 110p
US 2002052037 A1 20020502 (200234)
ADT WO 9828317 A2 WO 1997-US23936 19971219; AU 9857204 A AU 1998-57204 19971219; EP 948511 A2 EP 1997-953464 19971219, WO 1997-US23936 19971219; US 6159951 A Provisional US 1997-37998P 19970213, US 1997-982841 19971202; US 6248878 B1 Provisional US 1996-34444P 19961224, US 1997-975238 19971121; US 6251666 B1 Provisional US 1997-42464P 19970331, US 1998-48825 19980325; JP 2001507688 W WO 1997-US23936 19971219, JP 1998-529077 19971219; US 2002052037 A1 Provisional US 1997-42464P 19970331, Cont of US 1998-48825 19980325, US 2001-812186 20010319
FDT AU 9857204 A Based on WO 9828317; EP 948511 A2 Based on WO 9828317; JP 2001507688 W Based on WO 9828317; US 2002052037 A1 Cont of US 6251666
PRAI US 1997-42464P 19970331; US 1996-34444P 19961224; US 1997-37998P 19970213; US 1997-982841 19971202; US 1997-975238 19971121; US 1998-48825 19980325; US 2001-812186 20010319
AB WO 9828317 A UPAB: 19991122
Nucleoside and nucleotide derivatives that contain a 2'-O-NHR1 substituent (compounds (A)) or 2'-O-N=R3 substituent (compounds (B)) are new. R1 = hydrogen, aminoacyl, peptidyl, biotinyl, cholesteryl, alkyl, alkenyl, alkynyl, alkaryl, carbocyclic or heterocyclic aryl, amide, ester, or the residue of lipoic, retinoic, folic, ascorbic, nicotinic,

6-aminopenicillanic or 7-aminocephalosporanic acids; R3 = residue of **pyridoxal** (or its 5-phosphate), 13- or 9-cis retinal, alkyl, alkenyl, alkynyl, alkaryl, carbocyclic or heterocyclic aryl.

Also new are: (1) **nucleoside** or nucleotide derivatives (C) in which the nucleic acid base is 2-fluoropyridin-3-yl, pyridin-2-on-3-yl, pyridin-2-on-5-yl, pyridin-2-(4-nitrophenylethyl)-on-3-yl, pyridin-2-(4-nitrophenylethyl)-on-5-yl, 2-bromopyridin-5-yl, or 2-aminopyridin-5-yl;

(2) polynucleotides (D) containing at least one of (A)-(C); (3) a nucleic acid catalyst (E) containing at least one L-nucleotide substitution; and (4) mammalian cells containing (A), (B), (C), (D) or (E).

USE - (D) and (E) are modulators of gene expression, particularly for treatment of disease. Particularly they are ribozymes, but may also be antisense sequences, triplex-forming agents etc. The ribozymes may also be used diagnostically, e.g. to examine genetic drift and mutations in diseased cells, to detect specific RNA and to define the role of particular genes in disease progression. (A)-(C) are useful as antiviral (claimed) or anticancer (not claimed) agents, also intermediates in synthesis of (D), (E) and other oligonucleotides, e.g. probes and primers. (D) and (E) are administered, optionally complexed with cationic lipid or included in liposomes, to smooth muscle cells, e.g. via catheter, infusion pump etc., or by injection, orally etc. Also described is ex vivo delivery to cells and tissues.

ADVANTAGE - (E) are more resistant to **nuclease** than corresponding all-D-**analogues**, so have greater effect. The amino group in (A) allows conjugation to a wide variety of agents, by reaction with carbonyl compounds to form (B). Oxime formation is nearly quantitative and can be done in aqueous solution, and the products are stable over a wide pH range, are amphoteric and complexing agents for many metal ions. Incorporation of (B) into oligonucleotides can be used e.g. to improve cellular delivery, **nuclease** resistance, cell transport and localisation etc.

Dwg.0/25

L30 ANSWER 19 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 1997-362920 [33] WPIDS
CR 1993-196743 [24]; 1998-609233 [51]; 2002-535437 [57]
DNC C1997-116254
TI Nucleo monomers containing unsaturated pyrimidine base analogues - form oligomer duplexes or triplexes with nucleic acid under physiological conditions, and used in gene expression inhibition, diagnosis and **assay**.
DC A26 A96 B02 B03 B04 D16
IN FROEHLER, B; GUTIERREZ, A J; JONES, R J; MATTEUCCI, M; PUDLO, J; WAGNER, R
PA (ISIS-N) ISIS PHARM INC; (GILE-N) GILEAD SCI INC
CYC 2
PI US 5645985 A 19970708 (199733)* 104p
TW 393513 A 20000611 (200108)
ADT US 5645985 A CIP of US 1991-799824 19911126, CIP of US 1992-935444 19920825, CIP of US 1992-965941 19921023, US 1992-976103 19921125; TW 393513 A TW 1993-101747 19930308
FDT US 5645985 A CIP of US 5484908
PRAI US 1992-976103 19921125; US 1991-799824 19911126; US 1992-935444 19920825; US 1992-965941 19921023
AB US 5645985 A UPAB: 20020910
Nucleomonomer analogues of **uridine** of formula (III) and of cytosine of formula(IV), both containing an unsaturated group in the pyrimidine ring, are new. In the formula,
X = O or S;

R1 = H or a blocking group which is H-phosphonate, a phosphoramidite, an alkylphosphoramidite or FMOC; R2 = vinyl, 1-butenyl, 1-pentenyl, 1-hexenyl, 1-heptenyl, 1-octenyl, 1,3-pentadiynyl, 1-propynyl, 1-butynyl, 1-pentynyl, 3-methyl-1-butynyl, 3,3-dimethyl-1-butynyl, 3-buten-1-ynyl, bromovinyl, 1-hexynyl, 1-heptynyl, 1-octynyl, -C triple bond C-Z, or heteroaryl or (alkyn-1-yl)-heteroaryl both optionally ring C-substituted by oxygen or 1-4C alkyl or ring N-substituted by 1-4C alkyl; Z = 1-10C alkyl or haloalkyl;

PG = (H,H) or a protecting group;

R3 = H, OH, F, OMe, OEt, OPr, SMe, SEt, SPr, allyloxy or allylthio.

provided that when R3 = H or OH and both R1 = H, then R2 = Y-ethynyl, 2-pyrimidinyl, 2- or 4- imidazolyl, 2-, 4- or 5- thiazolyl, 4- or 5-oxazolyl or 3-pyrrolyl; and

Y = 2-, 3- or 4- pyridyl, 2-, 4- or 5-pyrimidinyl, triazinyl, 2- or 3-pyrrolyl, 2- or 3-furanyl, 2- or 3-thienyl, 2-, 4- or 5- thiazolyl, or 2-, 4- or 5-oxazolyl.

USE - (III) and (IV) are intermediates for formation of oligomers containing the above abnormal pyrimidine bases, which are **analogues** of the normal bases **uridine** (or thymine) and **cytidine**. These oligomers may have substitute unit linkages rather than the normal phosphate link, e.g., thiophosphate, sulphide, sulphone, carbamate, etc. The 5-substituent provides enhanced binding capacity in formation of duplexes and triplexes with single strand and double strand, respectively, RNA and DNA. Triplexes can indeed be formed at pH levels down to 7.0, i.e., under physiological pH conditions. The lipophilic R2 group provided by (III) and (IV) can also enhance cell permeation and uptake. The oligomers also show enhanced resistance to **nucleases** . The oligomers are used to form duplexes and triplexes as normal oligomers, for inhibition of gene expression, e.g. by their antisense configuration, for therapeutic or research purposes, and also in diagnosis to provide probes or primers for specific RNA or DNA.

Dwg.0/18

L30 ANSWER 20 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 1995-336716 [43] WPIDS
DNC C1995-148431
TI New substd. pyrimidine **nucleoside** derivs. - used for the prepn. of oligo-**nucleoside**(s) and oligo-nucleotide(s) used for binding RNA or DNA.
DC B03
IN ACEVEDO, O; COOK, P D; DUNKEL, M G
PA (ISIS-N) ISIS PHARM INC
CYC 48
PI WO 9524185 A1 19950914 (199543)* EN 44p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB HU JP KP KR KZ LK LU LV MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TT UA UZ VN
AU 9465503 A 19950925 (199601)
ADT WO 9524185 A1 WO 1994-US2652 19940311; AU 9465503 A AU 1994-65503 19940311, WO 1994-US2652 19940311
FDT AU 9465503 A Based on WO 9524185
PRAI WO 1994-US2652 19940311
AB WO 9524185 A UPAB: 19951102
Pyrimidine **nucleosides** of formula (I) and (II) are new. R5 = H or CH3; one of R2 and R4 is = O, =NH or -NH2, and the other is Q, =C(Ra)-Q, C(Ra)(Rb)C(Rc)(Rd)Q C(Ra)=C(Rc)-Q or Ctriple bondC-Q; Ra-Rd = H, SH, OH, NH2 or 1-20C alkyl or one of (Ra)(Rb) or (Cc)(Rd) = =O; Q = H, halo, 1-20C alkyl, 1-20C alkylamine, 1-20C alkyl-N-phthalimide, 1-20C alkyl-imidazole, 1-20C alkyl-bis-imidazole, imidazole, bis-imidazole, amine, N-phthalamide, 2-20C alkenyl, 2-20C alkynyl, OH, SH, keto,

carboxyl, nitrates, nitro, nitroso, nitrile, CF3, OCF3, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, azido, hydrazino, hydroxylamino, isocyanato, sulphoxide, sulphone, sulphide, disulphide, silyl, O-(hydroxyl protecting gp.). a leaving gp., a heterocycle, an intercalator, a reporter molecule, a conjugate, a polyamine, a polyamide, a polyethylene glycol, a polyether, a gp. that enhances the pharmacodynamic properties of oligonucleotides, a gp. that enhances the pharmacokinetic properties of oligonucleotides, a RNA cleaving moiety or a depurination enhancing gp.; X1, X2 = H, halo, OH, O-(hydroxyl protecting gp.), SH, carboxyl, nitrate, nitro, nitroso, nitrile, CF3, OCF3, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, azido, hydrazine, hydroxylamino, isocyanato, sulphoxide, sulphone, sulphide, disulphide, silyl, heterocyclic, alicyclic, carbocyclic, intercalators, reporter molecules, conjugates, polyamines, polyamides, polyethylene glycols, polyethers or gps. that enhance the pharmacodynamic or pharmacokinetic properties of oligonucleotides; T3, T5 = H, phosphate, an activated phosphate, a hydroxyl protecting gp. a **nucleoside**, a nucleotide an oligonucleotide or an oligonucleoside; provided that when T5 is a hydroxyl protecting gp. or together T3 and on of X1 or X2 is a hydroxyl protecting gp., then R2 is not CH3; and that when T3 and T5 are OH or O-benzoyl, then R2 is not CH2OC6H5; and that when R4 is Q, then Q is H, OH, SH, amino or H; J = N or CH; R'4 = =O, -NH or =NH+2; R'2 = Q, -C(Ra)-Q, C(Ra)(Rb)-C(Rc)(Rd)-Q, C(Ra)=C(Rc)-Q or Ctriple bondC-Q; the provisos do not apply in (II). Also claimed are oligonucleotides which contain at least one **nucleoside** of formula (I) where T3 and T5 are H, a **nucleoside** or an oligonucleoside and without the provisos.

USE - (I) and (II) and oligonucleosides and oligonucleotides contg. them can be used in diagnostics, therapeutics and as research reagents and **kits**. They can be used for selective binding of RNA or DNA. In partic. (I) can be used for treating an organism having a disease characterised by the undesired prodn. of a protein of for modulating the prodn. or activity of a protein in an organism (claimed).

ADVANTAGE - Oligonucleotides incorporating the cpds. are resistant to degradative **nucleases** and hybridise more strongly and with greater fidelity to RNA or DNA than known oligonucleotides or oligonucleotide **analogues**.

Dwg.0/1

L30 ANSWER 21 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 1994-333100 [41] WPIDS
CR 1991-237978 [32]; 1992-080013 [10]; 1992-096815 [12]; 1992-096911 [12]; 1992-415799 [50]; 1992-415800 [50]; 1993-018137 [02]; 1993-152175 [18]; 1993-152487 [18]; 1993-227263 [28]; 1993-303152 [38]; 1993-320768 [40]; 1994-026130 [03]; 1994-048786 [06]; 1994-135570 [16]; 1994-332803 [41]; 1994-333091 [41]; 1994-333094 [41]; 1994-333101 [41]; 1995-066911 [09]; 1995-115256 [15]; 1995-206893 [27]; 1995-215086 [28]; 1995-246328 [32]; 1995-292881 [38]; 1995-302445 [39]; 1995-402802 [51]; 1996-200879 [20]; 1997-011289 [01]; 1997-020468 [02]; 1997-042296 [04]; 1997-042838 [04]; 1997-363002 [33]; 1997-424765 [39]; 1998-008042 [01]; 1998-296838 [26]; 1999-024070 [02]; 1999-080503 [07]; 1999-080505 [07]; 1999-120005 [10]; 1999-120932 [10]; 1999-166721 [14]; 1999-214073 [18]; 1999-228583 [19]; 1999-394857 [33]; 1999-403817 [34]; 1999-404471 [34]; 1999-517980 [43]; 1999-539598 [45]; 1999-561076 [47]; 2000-072074 [06]; 2000-106010 [09]; 2000-237346 [20]; 2000-410235 [35]; 2000-586484 [55]; 2000-610851 [58]; 2001-025027 [03]; 2001-407099 [43]; 2001-528597 [58]; 2001-624246 [72]; 2002-054477 [07]; 2002-215022 [27]; 2002-517809 [55]; 2002-565044 [60]
DNC C1994-151535
TI New oligo-nucleotide analogues - having linkages contg. adjacent nitrogen atoms for resistance to degradative necklaces.

DC B04 D16
IN COOK, P D; SANGHVI, Y S
PA (ISIS-N) ISIS PHARM INC
CYC 19
PI WO 9422893 A1 19941013 (199441)* EN
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA JP
US 5792844 A 19980811 (199839)
ADT WO 9422893 A1 WO 1994-US3129 19940323; US 5792844 A CIP of US 1990-558663 19900727, CIP of US 1990-566836 19900813, CIP of US 1991-703619 19910521, CIP of WO 1992-US4294 19920521, CIP of US 1992-903160 19920624, Cont of US 1993-39979 19930330, US 1994-317289 19941003
FDT US 5792844 A CIP of US 5138045, CIP of US 5223618, CIP of US 5378825
PRAI US 1993-39979 19930330; US 1990-558663 19900727; US 1990-566836 19900813; US 1991-703619 19910521; WO 1992-US4294 19920521; US 1992-903160 19920624; US 1994-317289 19941003
AB WO 9422893 A UPAB: 20021007
Oligonucleotide analogues of formula (I) are new. In the formula, L1-L2-L3-L4 = CH2-NR1-NR2-CH2, CH2-CH2-NR1-NR2 or NR1-NR2-CH2-CH2; R1, R2 = H, alkyl or substd. alkyl having 1-10C, alkenyl or substd. alkenyl having 2-10C, alkynyl or substd. alkynyl having 2-10C alkaryl, substd. alkaryl, aralkyl or substd. aralkyl having 7-14C, alicyclic, heterocyclic, a reporter molecule, a RNA cleaving gp., a gp. for improving the pharmacokinetic properties of an oligonucleotide or a gp. for improving the pharmacodynamic properties of an oligonucleotide; Bx = a **nucleoside** base; Q = O, S, CH2, CHF or CF2; n = an integer greater than O; X = H, OH, 1-10C alkyl, substd. lower alkyl, alkaryl or aralkyl, F, Cl, Br, CN, CF3, OCF3, OCN, O-alkyl, S-alkyl, N-alkyl, O-alkenyl, S-alkenyl, N-alkenyl, SOCH3, SO2CH3, ONO2, NO2, N3, NH2, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino or substd. silyl, a RNA cleaving gp. or a gp. for improving the pharmacokinetic or pharmacodynamic properties of an oligonucleotide.
USE/ADVANTAGE - The oligonucleotide **analogues** can be used in therapeutics, diagnostics and research. They can be used for modulating the prodn. or activity of a protein in an organism, treating an organism having a disease characterised by the undesired prodn. of a protein or for **assaying** a sequence-specific nucleic acid (claimed). The cpds. are resistant to degradative **nucleases** and hybridise more strongly and with greater fidelity than known oligonucleotides or oligonucleotide **analogues**. They can be taken into cells by simple passive transport.
Dwg.0/2

L30 ANSWER 22 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 1994-333078 [41] WPIDS
DNC C1994-151513
TI New acyclic **nucleoside analogues** - used to prepare **nuclease** resistant oligo-nucleotide(s) used partic. for inhibiting gene expression.
DC B02 D16
IN COOK, P D; DELECKI, D J; GUINOSSO, C
PA (STER) STERLING WINTHROP INC; (SNFI) SANOFI; (SNFI) SANOFI SA
CYC 31
PI WO 9422864 A1 19941013 (199441)* EN 37p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU BR CA CZ FI HU JP KR NO NZ RU SK UA
AU 9464493 A 19941024 (199505)
EP 691968 A1 19960117 (199608) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5576427 A 19961119 (199701) 13p

JP 08508492 W 19960910 (199704) 35p
EP 691968 B1 19970716 (199733) EN 31p
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69404289 E 19970821 (199739)
ES 2107205 T3 19971116 (199801)

ADT WO 9422864 A1 WO 1994-US2995 19940321; AU 9464493 A AU 1994-64493 19940321; EP 691968 A1 EP 1994-912266 19940321, WO 1994-US2995 19940321; US 5576427 A Cont of US 1993-40326 19930330, US 1995-452196 19950526; JP 08508492 W JP 1994-522133 19940321, WO 1994-US2995 19940321; EP 691968 B1 EP 1994-912266 19940321, WO 1994-US2995 19940321; DE 69404289 E DE 1994-604289 19940321, EP 1994-912266 19940321, WO 1994-US2995 19940321; ES 2107205 T3 EP 1994-912266 19940321

FDT AU 9464493 A Based on WO 9422864; EP 691968 A1 Based on WO 9422864; JP 08508492 W Based on WO 9422864; EP 691968 B1 Based on WO 9422864; DE 69404289 E Based on EP 691968, Based on WO 9422864; ES 2107205 T3 Based on EP 691968

PRAI US 1993-40326 19930330; US 1995-452196 19950526

AB WO 9422864 A UPAB: 19970530

Nucleoside analogues of formula (I) are new. In the formula R1 = H or a blocking gp. that is compatible with oligonucleotide (ON) synthesis; R2 = H or Me; R3 = H or -P(R4)(OR5); R4 = Cl, 4-nitroimidazole, imidazole, tetrazole, triazole or di(lower alkyl)amino; R5 = Me, 2-cyanoethyl or 2,2,2-trichloroethyl; n = 0-2; x = O, S or NR6; R6 = H or lower alkyl; Q = gp. (i) or (ii); R7 = lower alkyl and R8 = H, benzoyl, anisoyl or lower alkylcarbonyl.

Also claimed is a cpd. comprising an ON sequence of 6-200 bases in which one or more **nucleosides** are replaced by a residue of formula (II).

USE - (II) can inhibit nuclease degradation of the ON (claimed). The ONs can be used for the inhibition of gene expression (claimed) as antisense agents, in nucleic acid sequencing and diagnostic **assays**.

Dwg.0/0

L30 ANSWER 23 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 1994-332803 [41] WPIDS
CR 1991-237978 [32]; 1992-080013 [10]; 1992-096815 [12]; 1992-096911 [12]; 1992-415799 [50]; 1992-415800 [50]; 1993-018137 [02]; 1993-152175 [18]; 1993-152487 [18]; 1993-227263 [28]; 1993-303152 [38]; 1993-320768 [40]; 1994-026130 [03]; 1994-048786 [06]; 1994-135570 [16]; 1994-333091 [41]; 1994-333094 [41]; 1994-333100 [41]; 1994-333101 [41]; 1995-066911 [09]; 1995-115256 [15]; 1995-206893 [27]; 1995-215086 [28]; 1995-246328 [32]; 1995-292881 [38]; 1995-302445 [39]; 1995-402802 [51]; 1996-200879 [20]; 1997-011289 [01]; 1997-020468 [02]; 1997-042296 [04]; 1997-042838 [04]; 1997-363002 [33]; 1997-424765 [39]; 1998-008042 [01]; 1998-296838 [26]; 1999-024070 [02]; 1999-080503 [07]; 1999-080505 [07]; 1999-120005 [10]; 1999-120932 [10]; 1999-166721 [14]; 1999-214073 [18]; 1999-228583 [19]; 1999-394857 [33]; 1999-403817 [34]; 1999-404471 [34]; 1999-517980 [43]; 1999-539598 [45]; 1999-561076 [47]; 2000-072074 [06]; 2000-106010 [09]; 2000-237346 [20]; 2000-410235 [35]; 2000-586484 [55]; 2000-610851 [58]; 2001-025027 [03]; 2001-407099 [43]; 2001-528597 [58]; 2001-624246 [72]; 2002-054477 [07]; 2002-215022 [27]; 2002-517809 [55]; 2002-565044 [60]
DNC C1994-151323
TI New oligo-nucleotide **analogues** - having linkages contg. adjacent oxygen and nitrogen atoms for resistance to degradative **nuclease** (s).
DC B04 D16
IN COOK, P D; SANGHVI, Y S
PA (ISIS-N) ISIS PHARM INC
CYC 19

PI WO 9422454 A1 19941013 (199441)* EN 128p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA JP
US 5489677 A 19960206 (199612) 43p
ADT WO 9422454 A1 WO 1994-US3313 19940325; US 5489677 A CIP of US 1990-558663 19900727, CIP of US 1990-566836 19900819, CIP of US 1991-703619 19910521, CIP of WO 1992-US4294 19920521, CIP of US 1992-903160 19920624, US 1993-40526 19930331
FDT US 5489677 A CIP of US 5138045, CIP of US 5223618, CIP of US 5378825
PRAI US 1993-40526 19930331; US 1990-558663 19900727; US 1990-566836 19900819; US 1991-703619 19910521; WO 1992-US4294 19920521; US 1992-903160 19920624
AB WO 9422454 A UPAB: 20021007
Oligonucleotide analogues of formula (I) are new. In the formula, L1-L2-L3-L4 = CH2-O-NR-CH2, CH2-NR-O-CH2, O-NR-CH2-CH2, CH2-CH2-NR-O, CH2-CH2-O-NR or NR-O-CH2-CH2; R = H, alkyl or substd. R = H, alkyl or substd. alkyl having 1-10C, alkenyl or substd. alkenyl having 2-10C, alkynyl or substd. alkynyl having 2-10C aralkyl having 7-14C, alicyclic, heterocyclic, a reporter molecule, a RNA cleaving gp., a gp. for improving the pharmacokinetic properties of an oligonucleotide or a gp. for improving the pharmacodynamic properties of an oligonucleotide; Bx = a **nucleoside** base; Q = O, S, CH2 or CF2; n = an integer greater than O; X = H, OH, 1-10C alkyl, substd. lower alkyl, alkaryl or aralkyl, F, Cl, Br, CN, CF3, OCF3, OCN, O-alkyl, S-alkyl, N-alkyl, O-alkenyl, S-alkenyl, N-alkenyl, SOCH3, SO2CH3, ONO2, NO2, N3, NH2, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino or substd. silyl, a RNA cleaving gp., a gp. for improving the pharmacokinetic properties of an oligonucleotide or a gp. for improving the pharmacodynamic properties of an oligonucleotide.

USE/ADVANTAGE - The oligonucleotide **analogues** can be used in therapeutics, diagnostics and research. They can be used for modulating the prodn. or activity of a protein in an organism, treating an organism having a disease characterised by the undesired prodn. of a protein or **assaying** a sequence-specific nucleic acid (claimed). The cpds. are resistant to degradative **nucleases** and hybridise more strongly and with greater fidelity than known oligonucleotides or oligonucleotides or oligonucleotide **analogues**. They can be taken into cells by simple passive transport.
Dwg.0/2

L30 ANSWER 24 OF 24 WPIDS (C) 2002 THOMSON DERWENT
AN 1994-026130 [03] WPIDS
CR 1991-237978 [32]; 1992-080013 [10]; 1992-096815 [12]; 1992-096911 [12]; 1992-415799 [50]; 1992-415800 [50]; 1993-018137 [02]; 1993-152175 [18]; 1993-152487 [18]; 1993-227263 [28]; 1993-303152 [38]; 1993-320768 [40]; 1994-048786 [06]; 1994-135570 [16]; 1994-332803 [41]; 1994-333091 [41]; 1994-333094 [41]; 1994-333100 [41]; 1994-333101 [41]; 1995-066911 [09]; 1995-115256 [15]; 1995-206893 [27]; 1995-215086 [28]; 1995-246328 [32]; 1995-292881 [38]; 1995-302445 [39]; 1995-402802 [51]; 1996-200879 [20]; 1997-011289 [01]; 1997-020468 [02]; 1997-042296 [04]; 1997-042838 [04]; 1997-363002 [33]; 1997-424765 [39]; 1998-008042 [01]; 1998-296838 [26]; 1999-024070 [02]; 1999-080503 [07]; 1999-080505 [07]; 1999-120005 [10]; 1999-120932 [10]; 1999-166721 [14]; 1999-214073 [18]; 1999-228583 [19]; 1999-394857 [33]; 1999-403817 [34]; 1999-404471 [34]; 1999-517980 [43]; 1999-539598 [45]; 1999-561076 [47]; 2000-072074 [06]; 2000-106010 [09]; 2000-237346 [20]; 2000-410235 [35]; 2000-586484 [55]; 2000-610851 [58]; 2001-025027 [03]; 2001-388462 [41]; 2001-407099 [43]; 2001-528597 [58]; 2001-624246 [72]; 2002-054477 [07]; 2002-215022 [27]; 2002-517809 [55]; 2002-565044 [60]
DNC C1994-012066

TI New macromolecules which mimic oligo nucleotide(s) with improved nuclease resistance - by replacing inter-sugar phosphate link by hetero-atomic chain, used in anti-sense therapy and diagnostics.
DC A96 B03 D16
IN COOK, P D; SANGHVI, Y S
PA (ISIS-N) ISIS PHARM INC
CYC 42
PI WO 9400467 A1 19940106 (199403)* EN 90p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AU BB BG BR CA CZ FI HU JP KP KR LK MG MN MW NO NZ PL RO RU SD SK UA
AU 9343830 A 19940124 (199420)
EP 649429 A1 19950426 (199521) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 07507563 W 19950824 (199542)
EP 649429 A4 19960410 (199642)
US 5623070 A 19970422 (199722) 27p
US 5777092 A 19980707 (199834)
JP 2879973 B2 19990405 (199919) 40p
ADT WO 9400467 A1 WO 1993-US4770 19930519; AU 9343830 A AU 1993-43830 19930519; EP 649429 A1 EP 1993-914006 19930519, WO 1993-US4770 19930519; JP 07507563 W WO 1993-US4770 19930519, JP 1994-502345 19930519; EP 649429 A4 EP 1993-914006 ; US 5623070 A CIP of US 1990-558663 19900727, CIP of US 1990-566836 19900813, CIP of US 1991-703619 19910521, Cont of US 1992-903160 19920624, US 1995-395168 19950227; US 5777092 A CIP of US 1990-558663 19900727, CIP of US 1990-566836 19900813, CIP of US 1991-703619 19910521, CIP of WO 1992-US4294 19920521, Cont of US 1992-903160 19920624, Div ex US 1995-395168 19950227, US 1997-795282 19970204; JP 2879973 B2 WO 1993-US4770 19930519, JP 1994-502345 19930519
FDT AU 9343830 A Based on WO 9400467; EP 649429 A1 Based on WO 9400467; JP 07507563 W Based on WO 9400467; US 5623070 A CIP of US 5138045, CIP of US 5223618, CIP of US 5378825; US 5777092 A CIP of US 5138045, CIP of US 5223618, CIP of US 5378825, Div ex US 5623070; JP 2879973 B2 Previous Publ. JP 07507563, Based on WO 9400467
PRAI US 1992-903160 19920624; US 1990-558663 19900727; US 1990-566836 19900813; US 1991-703619 19910521; US 1995-395168 19950227; WO 1992-US4294 19920521; US 1997-795282 19970204
AB WO 9400467 A UPAB: 20021007
(A) Oligonuclotide mimicking macromolecules, at least a portion of which is of structure (I), are new. L1-L4 represent the alternatives; (i) one of L1, L2 = O or S, the other is NR, L3 = CH2 and L4 = bond or CR'R''; (ii) one of L3, L4 = O or S, the other = NR L2 = CH2, and L1 = bond or CR'R''; (iii) one of L1, L4 = O, S, or NR, the other = CR'R'' and L2L3 together = CH2; (iv) L1-L4 together = ON=CHCH2 or CH2CH=NO; (v) L1 = O, L2 = N, L3 = CH2, and L4 = C or CH; and L2-L4, together with at least 2 additional C or hetero atoms, forms a 5 or 6 membered ring; (vi) L1 = C or CH, L2 = CH, L3 = N, and L4 = O; and L1-L3 together with at least 2 additional C or hetero atoms, form a 5 or 6 membered ring; R = H, or 1-10C alkyl, 2-10C alkenyl, or 2-10C alkynyl (all opt. substd.) 7-14C alkaryl or aralkyl alicyclic, heterocyclic, a reporter gp., an RNA cleaving gp. , or a gp. for improving the pharmacodynamic or pharmacokinetic properties of (I); R', R'' = H; or R' = H, R'' = OR; or R'R'' together = O; X = H, OR, SR, NHR, F, Cl, Br, CN, CF3, OCF3, OCN, SOMe, SO2Me, ONO2, NO2, N3, NH2, heterocycloalkyl, aminoalkylamino, polyalkylamino, substd. silyl, a reporter gp., an RNA cleaving gp., or a gp. for improving the pharmacodynamic or pharmacokinetic properties of (I); Q = O or CH2; n = an integer; and Bx = a heterocyclic base.

(B) **Nucleosides** of formula (II) are new: either Y1 = O, Y2 = H or R''', and Z = aminooxy or phthalimidooxy; or Y1 = CH, Y2 = aminooxy, alkylamino, aminohydroxyalkyl, alkenyl or oxoalkyl, and Z = H,

OH, OR''', amino, methyleneamino, or phthalimido; and X' = H or OH.

(C) Dinucleosides (III) in which the units are linked through the 3' and 4' positions by the linkage L1-L2-L3-L4, with definitions as for (I) are new.

USE/ADVANTAGE - Structures contg. (I) are capable of modulating the activity of DNA and RNA. By replacing the phosphate inter-sugar linkages of normal oligonucleotides, the mimics are resistant to **nucleases**, and also have enhanced cellular uptake and efficacy. They have satisfactory hybridisation properties for antisense therapeutics, diagnostics, and as research reagents and **kits**. Thus, organisms having a disease characterised by undesired prodn. of a protein e.g, 5-lipoxygenase, can be treated. In diagnostics, specific mRNA expression in tissues, or of abnormal or mutant RNA, can be **determined**. Sequence-specific nucleic acids can be **assayed**.

Dwg.0/0